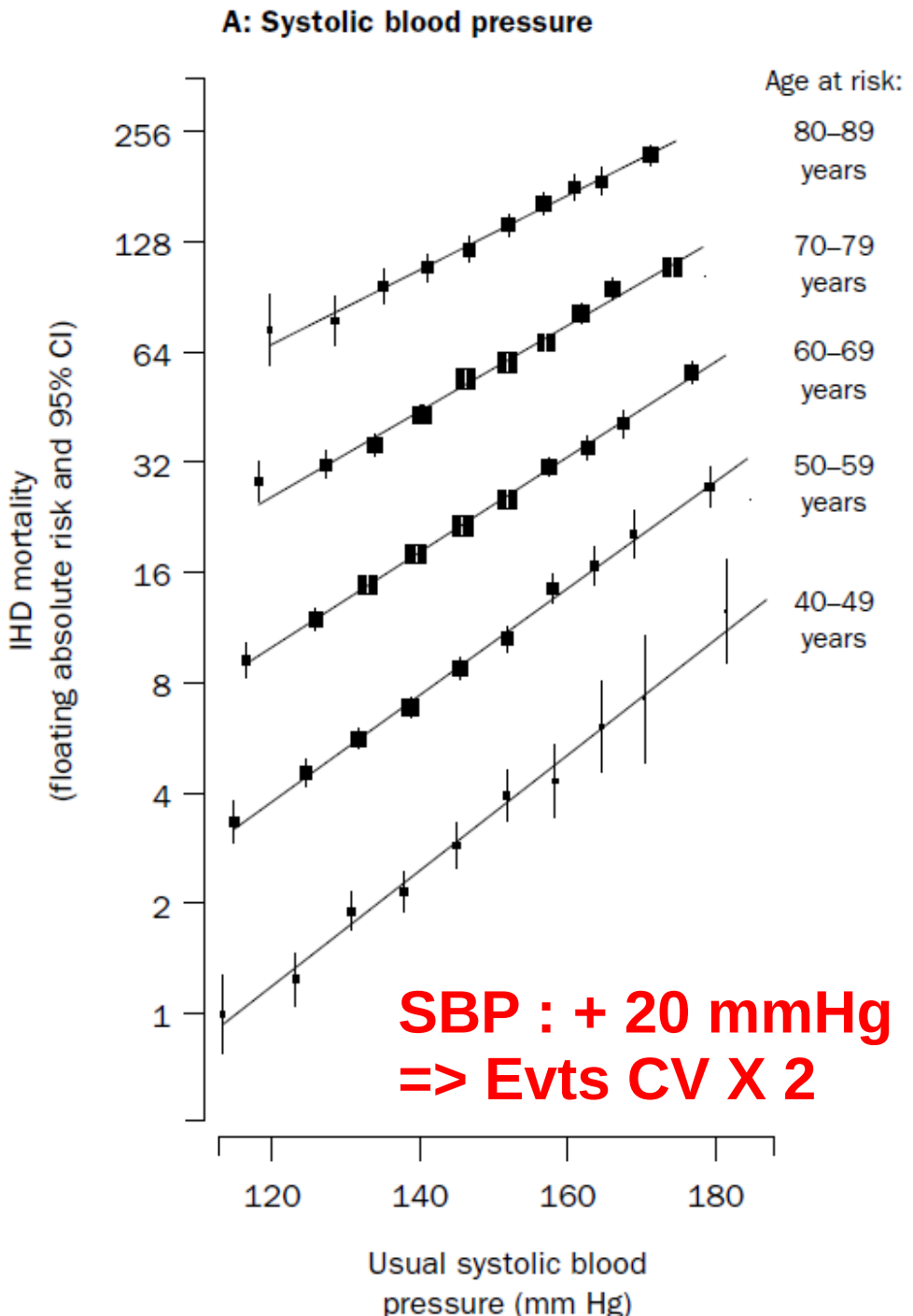
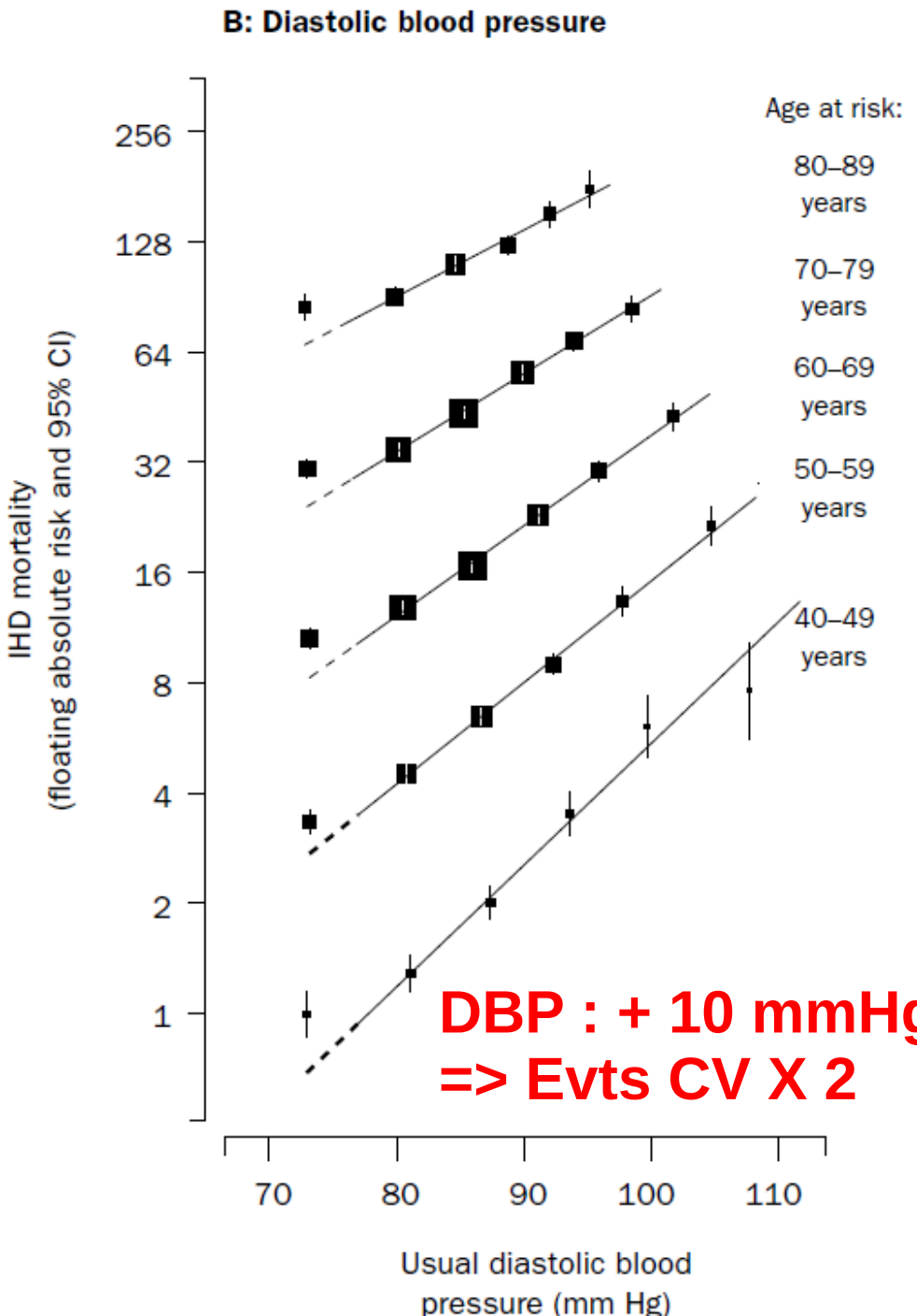
# Circulation Coronaire, Coronaropathie et Hypertension Artérielle

**Olivier Ormezzano**

**DIU**
**Hypertension artérielle, risque cardiovasculaire et rénal.**
***Janvier 2019***

**Age-specific relevance of usual blood pressure to vascular mortality: a metaanalysis of individual datafor one million adults in 61 prospective.** *Lewington et al. Lancet 2002*



**Mr FJ** 63 ans.

Suivi médicale très irrégulier…

**Facteurs de risque** une hypertension artérielle ancienne, une dyslipidémie, une hyperglycémie limite. Surcharge pondérale 90Kg/1,80m.

**ATCD :** Il y a 6 mois, il avait présenté un passage en FA rapide dans un contexte de poussées tensionnelles réduite en rythme sinusal par CORDARONE.

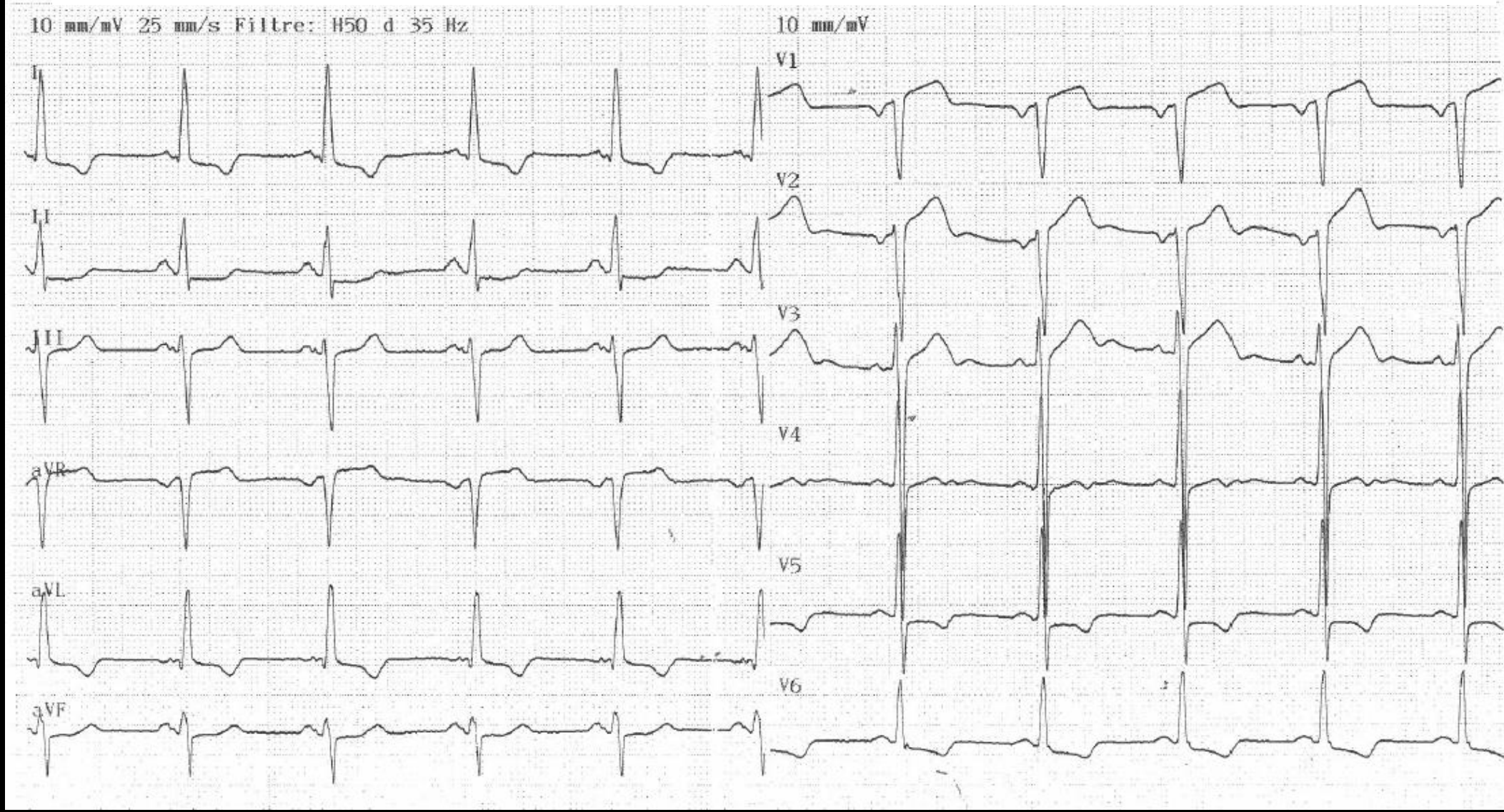
**A l'examen ce jour**, Mr FJ ne décrit pas de symptomatologie notable. L'auscultation est sans particularité. La pression artérielle est retrouvée à 167 /90 mm Hg. Pds 90 kg pour 1,80 m.

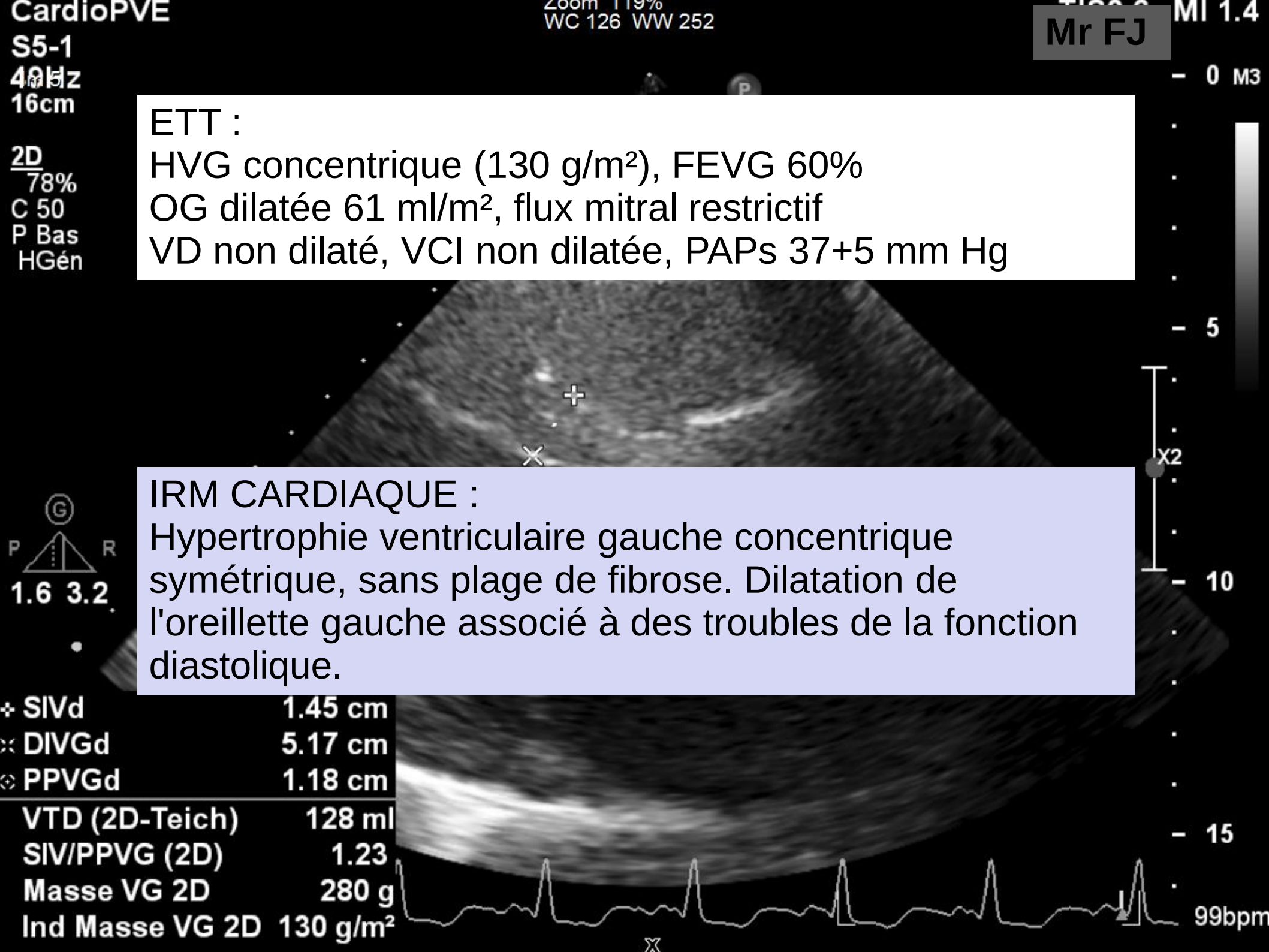
**Traitement :**
PERINDOPRIL 8mg/j, AMLODIPINE 10mg, BISOPROLOL 2.5mg, INDAPAMIDE 1.5mg, PRAVASTATINE 20mg/J, RIVAROXABAN

**Sokolow–Lyon index (SV1 + RV5/V6) >3.5 mV?**

**RDI > 13 mm  RaVL >1.1 mV  (RI - RIII) + (SIII - SI) > 17 mm**

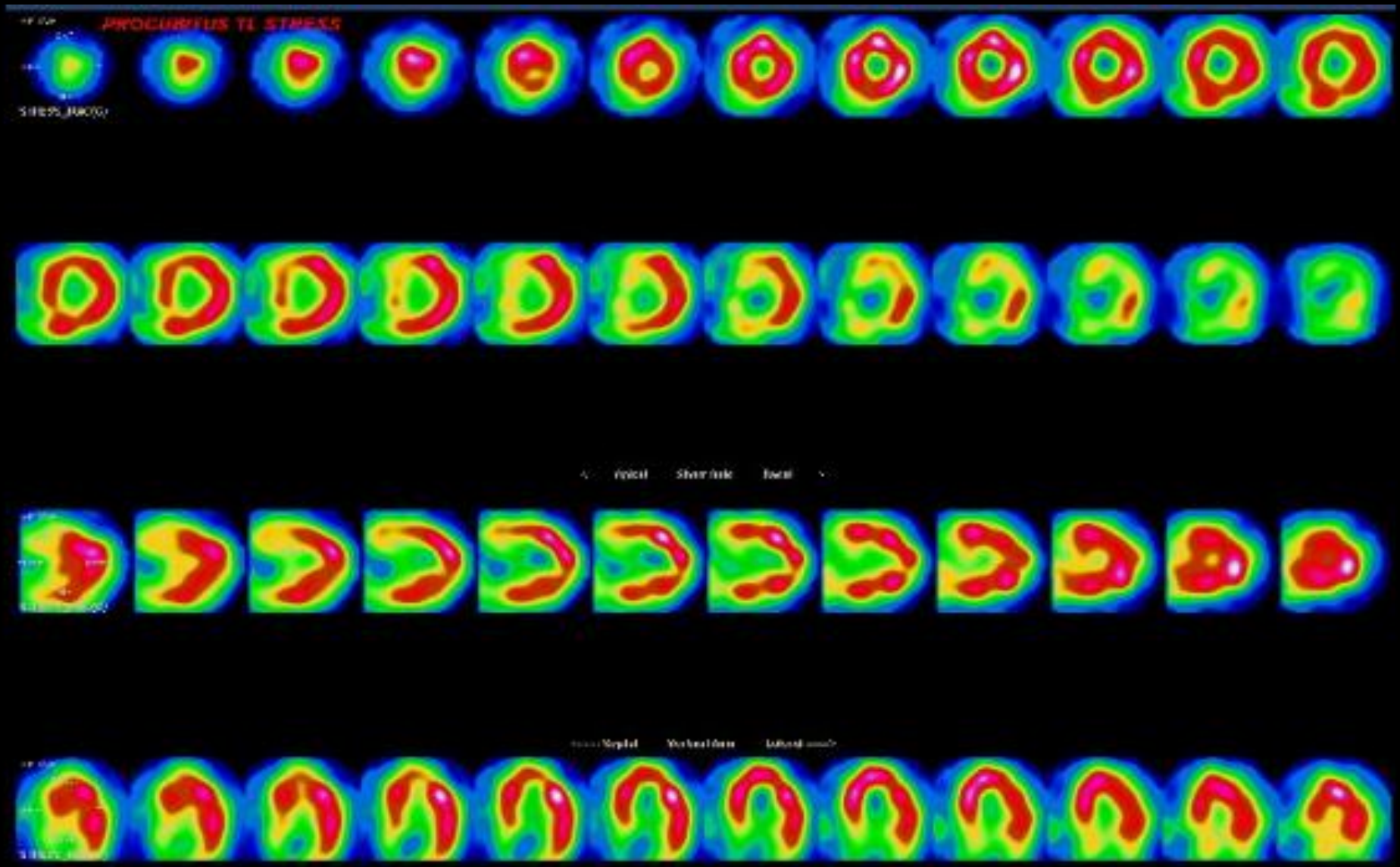
**Surcharge ventriculaire**



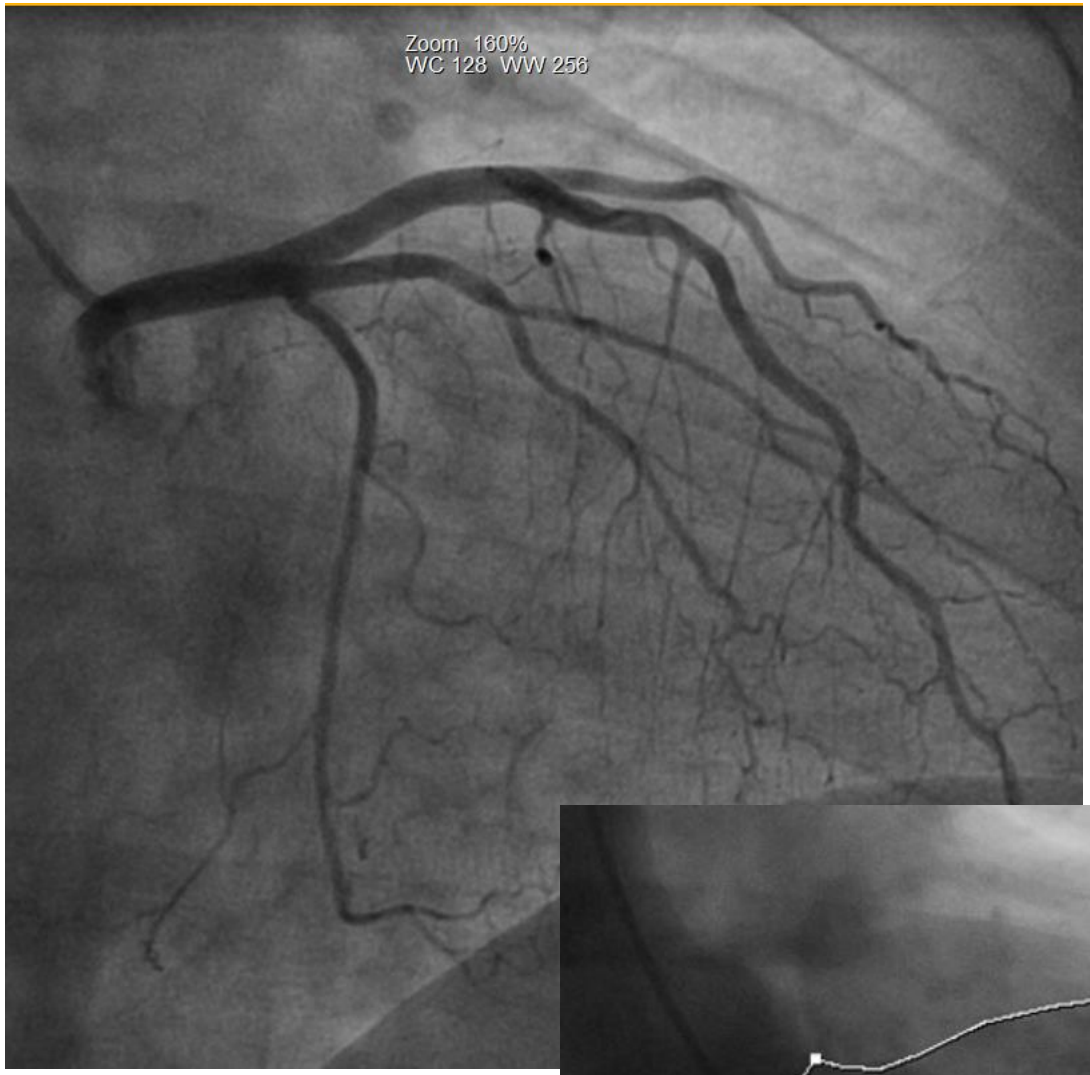


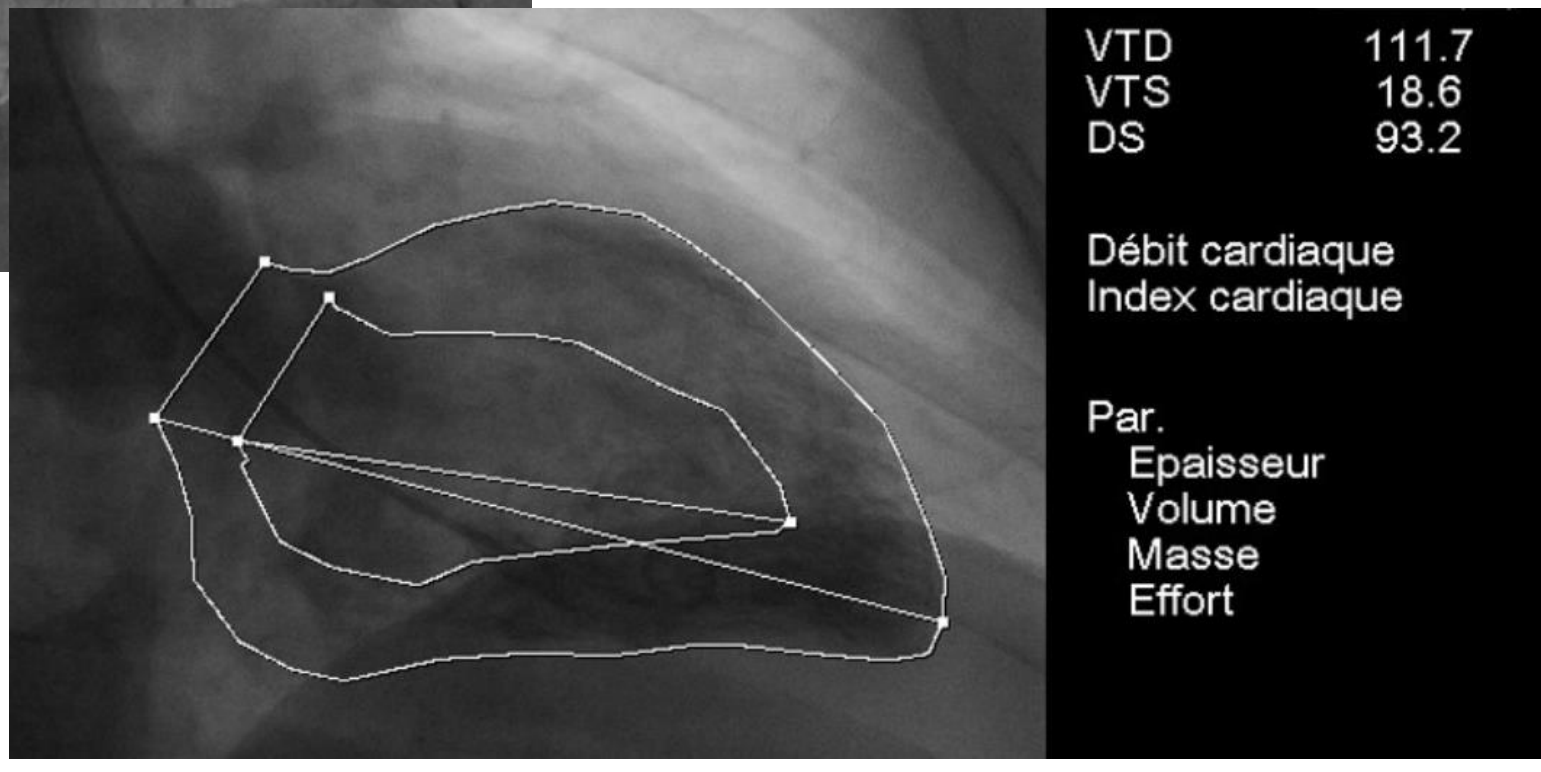

ETT :
HVG concentrique (130 g/m²), FEVG 60%
OG dilatée 61 ml/m², flux mitral restrictif
VD non dilaté, VCI non dilatée, PAPs 37+5 mm Hg

IRM CARDIAQUE :
Hypertrophie ventriculaire gauche concentrique symétrique, sans plage de fibrose. Dilatation de l'oreillette gauche associé à des troubles de la fonction diastolique.



Après PERSANTINE la fixation du Thallium 201 apparait un peu hétérogène mais sans hypofixation systématisée bien franche. En tomoscintigraphie synchronisée à l'ECG, la fonction ventriculaire gauche globale au repos et sous PERSANTINE est satisfaisante.
CONCLUSION : Perfusion myocardique un peu hétérogène sous stress, sans hypoperfusion systématisée franche.

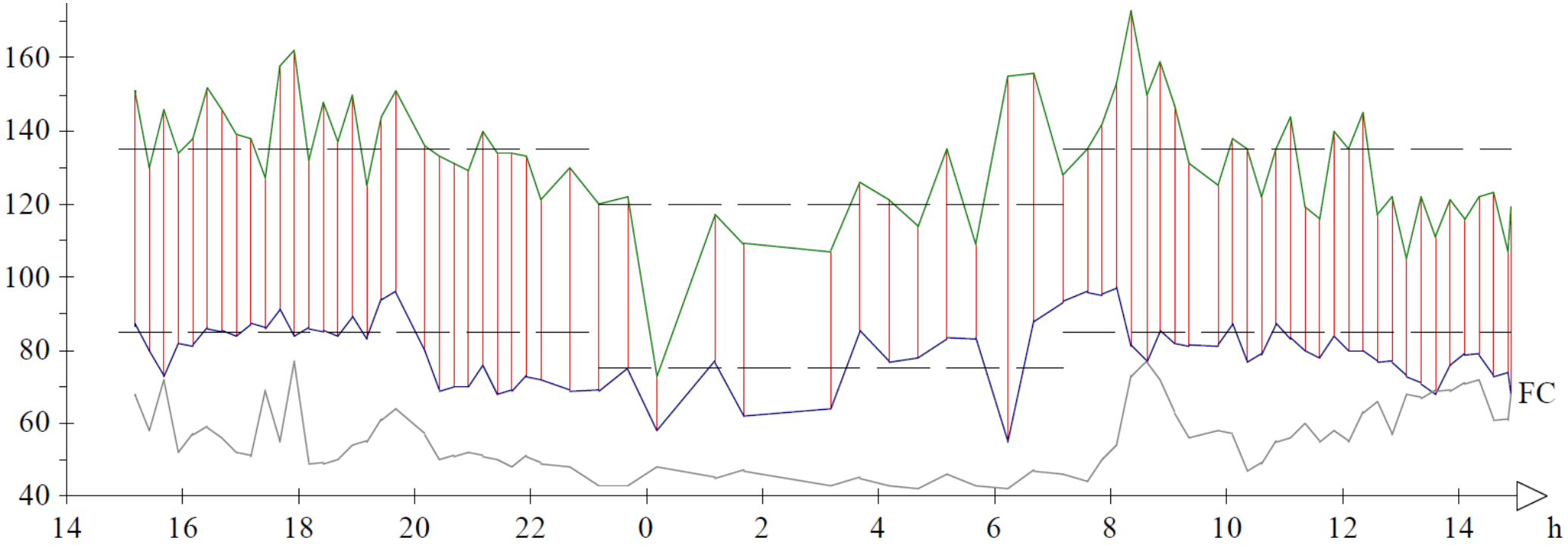

Zoom 160%
WC 128 WW 256


VTD 111.7
VTS 18.6
DS 93.2
Débit cardiaque
Index cardiaque
Par.
Epaisseur
Volume
Masse
Effort

# Mr FJ

| | Jour et nuit (73) | | | | | | (60) | | | | | | (13) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sys | Dia | Moy | Diff | FC | QKd | Sys | Dia | Moy | Diff | FC | QKd | Sys | Dia | Moy | Diff | FC | QKd |
| min. | 73 | 55 | 63 | 15 | 42 | 177 | 105 | 68 | 82 | 32 | 44 | 177 | 73 | 55 | 63 | 15 | 42 | 202 |
| max. | 173 | 97 | 130 | 100 | 77 | 247 | 173 | 97 | 116 | 92 | 77 | 247 | 156 | 88 | 130 | 100 | 48 | 237 |
| **moy.** | **132** | **79** | **98** | **53** | **56** | **219** | **135** | **81** | **99** | **54** | **58** | **218** | **120** | **73** | **92** | **47** | **44** | **220** |
| médian | 133 | 80 | 97 | 51 | 55 | 220 | 134 | 80 | 98 | 54 | 56 | 220 | 120 | 77 | 91 | 44 | 43 | 220 |
| écart | 16 | 9 | 10 | 14 | 9 | 15 | 14 | 8 | 8 | 12 | 8 | 15 | 20 | 10 | 16 | 20 | 2 | 10 |
| seuil | 135/120 | 85/75 | 102/90 | 50/45 | 90/80 | 200/180 | 135 | 85 | 102 | 50 | 90 | 200 | 120 | 75 | 90 | 45 | 80 | 180 |
| **%>** | **51** | **36** | **45** | **63** | **0** | **90** | **50** | **30** | **40** | **67** | **0** | **88** | **54** | **62** | **69** | **46** | **0** | **100** |

Variation JN : - 11,5 % pour la PAS et -9,9 % Pour la PAD



## *Hypertension*

## => *Anomalies Structurelles et/ou Fonctionnelles*

**1- Artères Coronaires Épicardiques**

**2- Petites Artères et Artérioles**

**3- Capillaires**

# *Hypertension*

## => *Anomalies Structurelles et/ou Fonctionnelles*

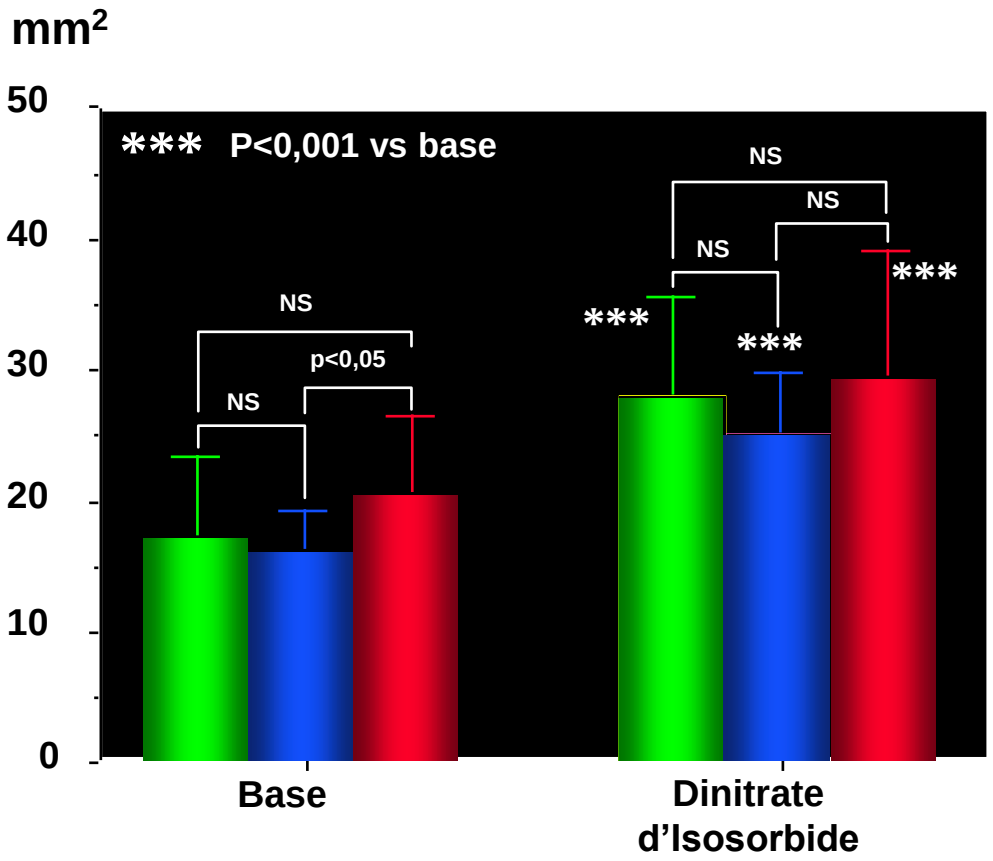
**1- Artères Coronaires Épicardiques**

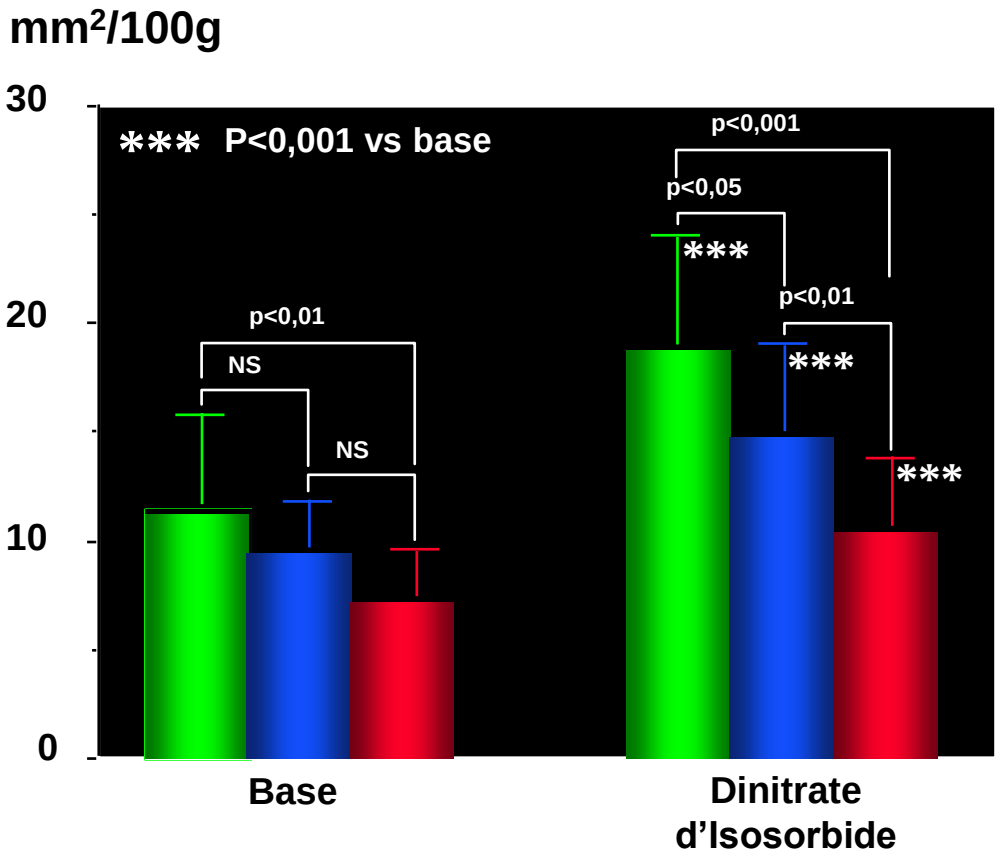
**2- Petites Artères et Artérioles**

**3- Capillaires**

# Pas de remodelage excentrique des artères coronaires chez l'hypertendu

## *Surface de Section (IVA + Cx)*




Sujets Témoins

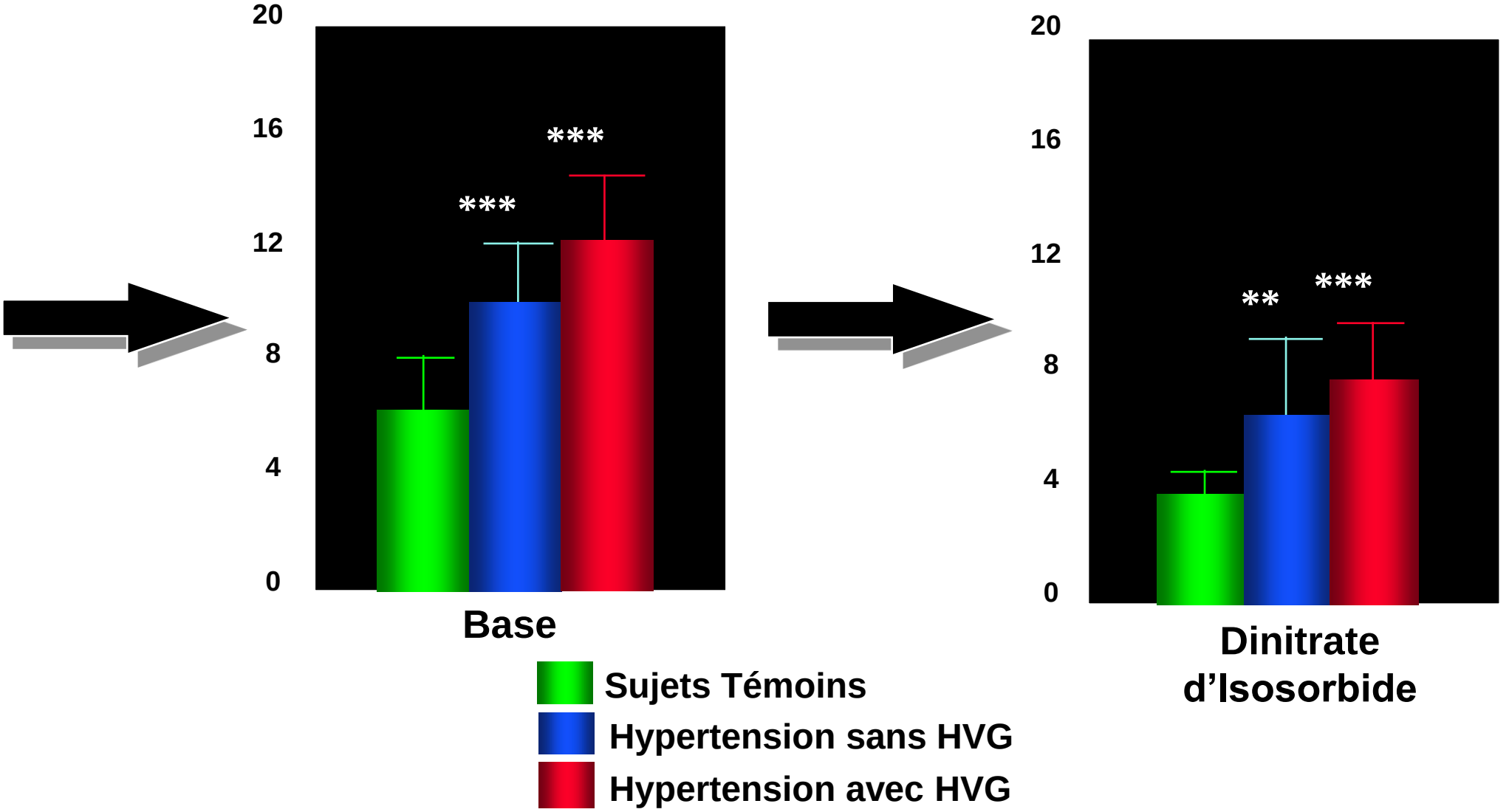
Hypertension sans HVG

Hypertension avec HVG

Nitenberg & Antony. J Am Coll Cardiol 1996; 27: 115-123.

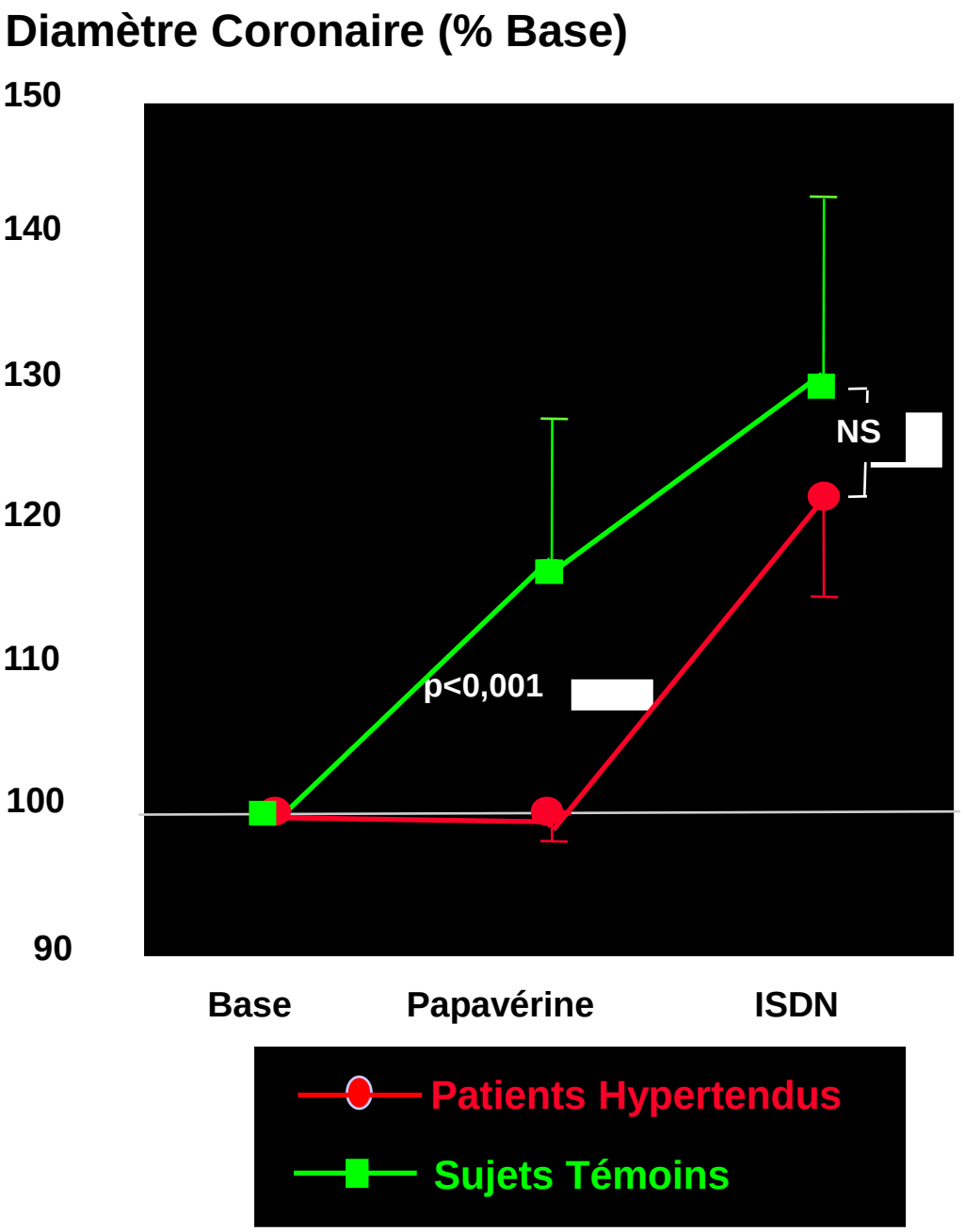
**Pas de remodelage excentrique des artères coronaires chez l'hypertendu**
**⇒ Augmentation de la vitesse du flux intracoronaire**
**⇒ augmentation des contraintes de cisaillement longitudinal**

## Vitesse d'Écoulement Intracoronaire (cm/sec)



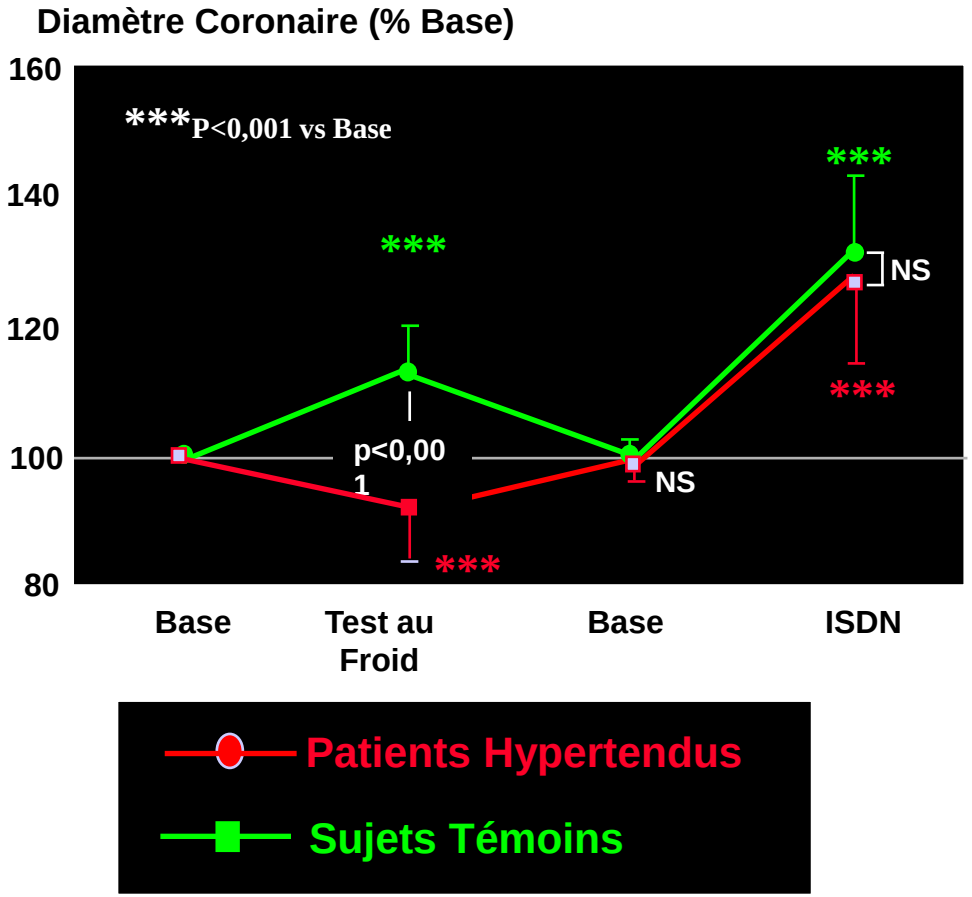

Nitenberg & Antony. J Am Coll Cardiol 1996; 27: 115-123.

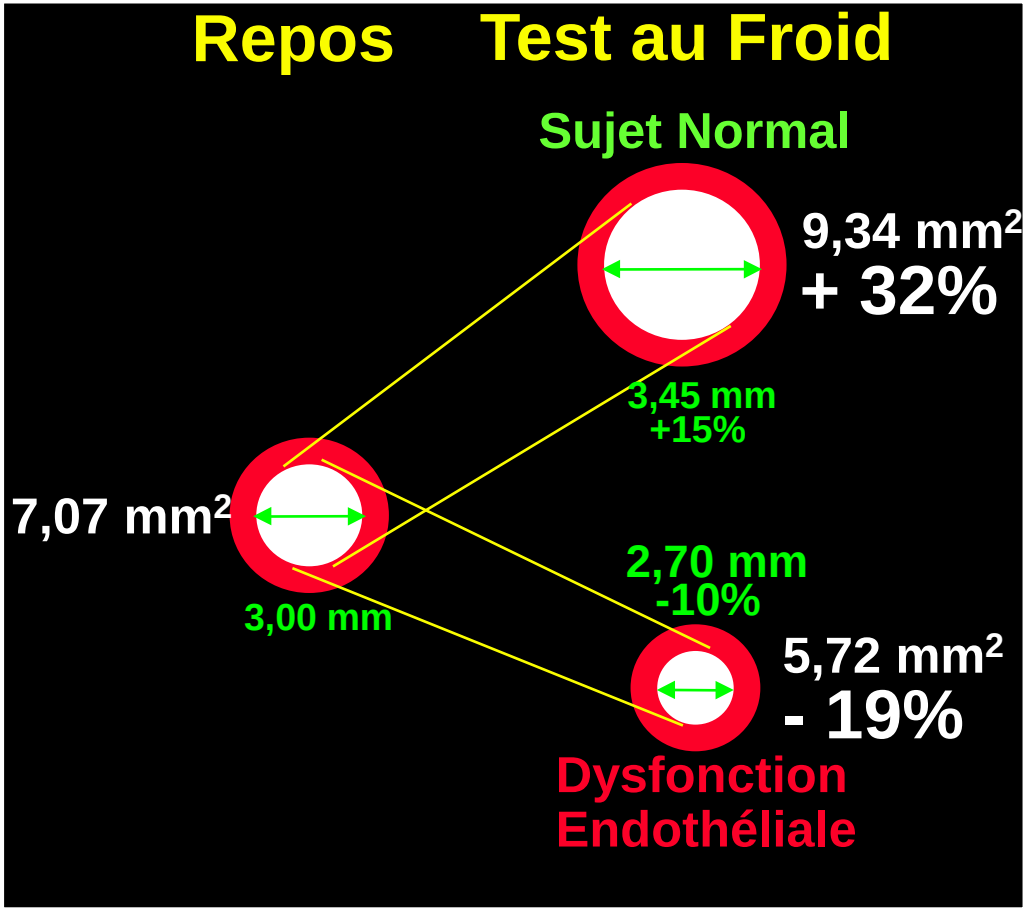
# Dysfonction endothéliale : absence de vasodilatation flux dépendant




Antony et coll. Circulation 1995; 91: 1624-1628.

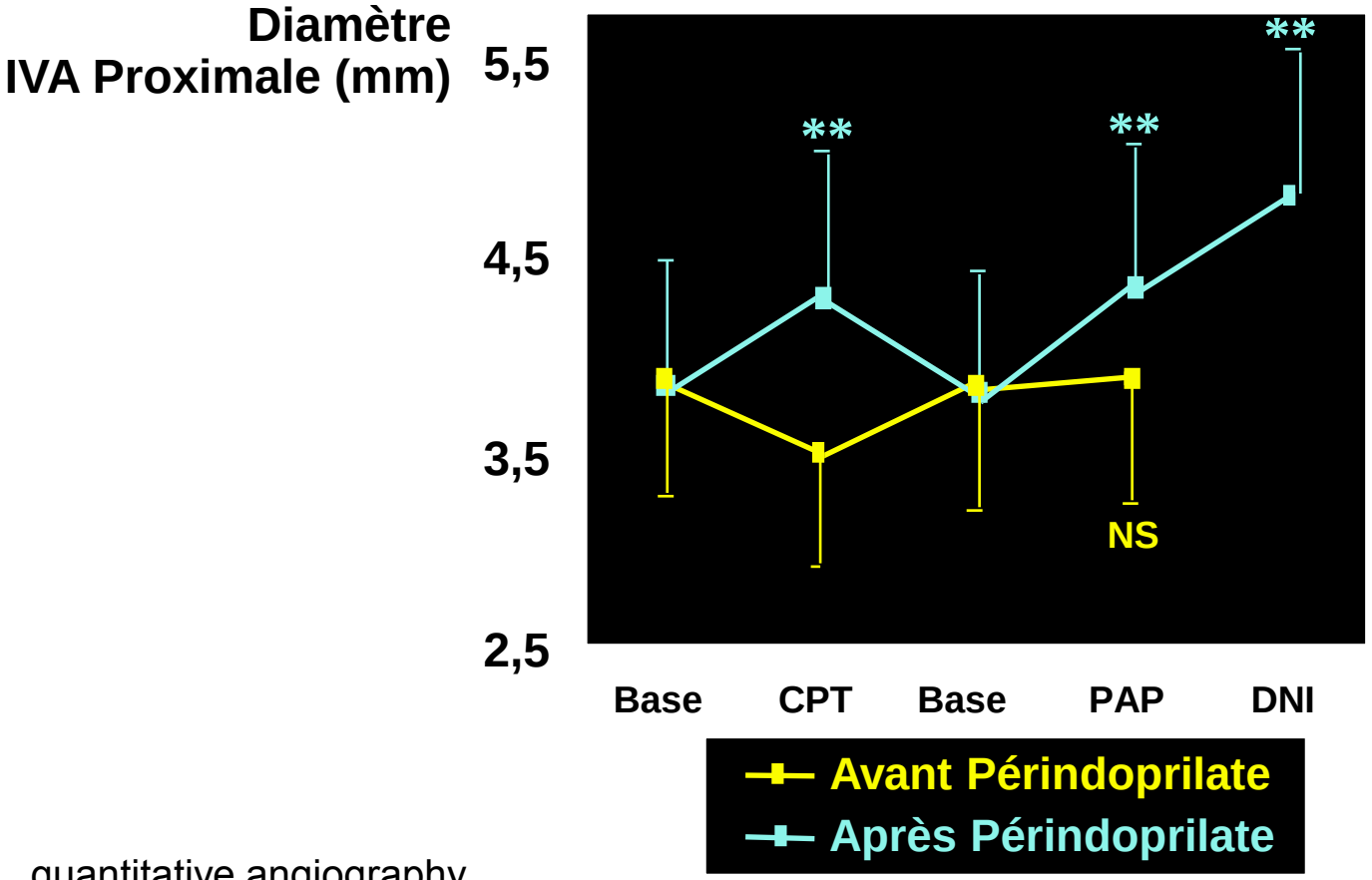
# Dysfonction endothéliale :
# Vasoconstriction paradoxale au froid
# Mais conservation de la vasodilatation endothélium indépendant




Antony et coll. Hypertension 1994; 24: 212-219.

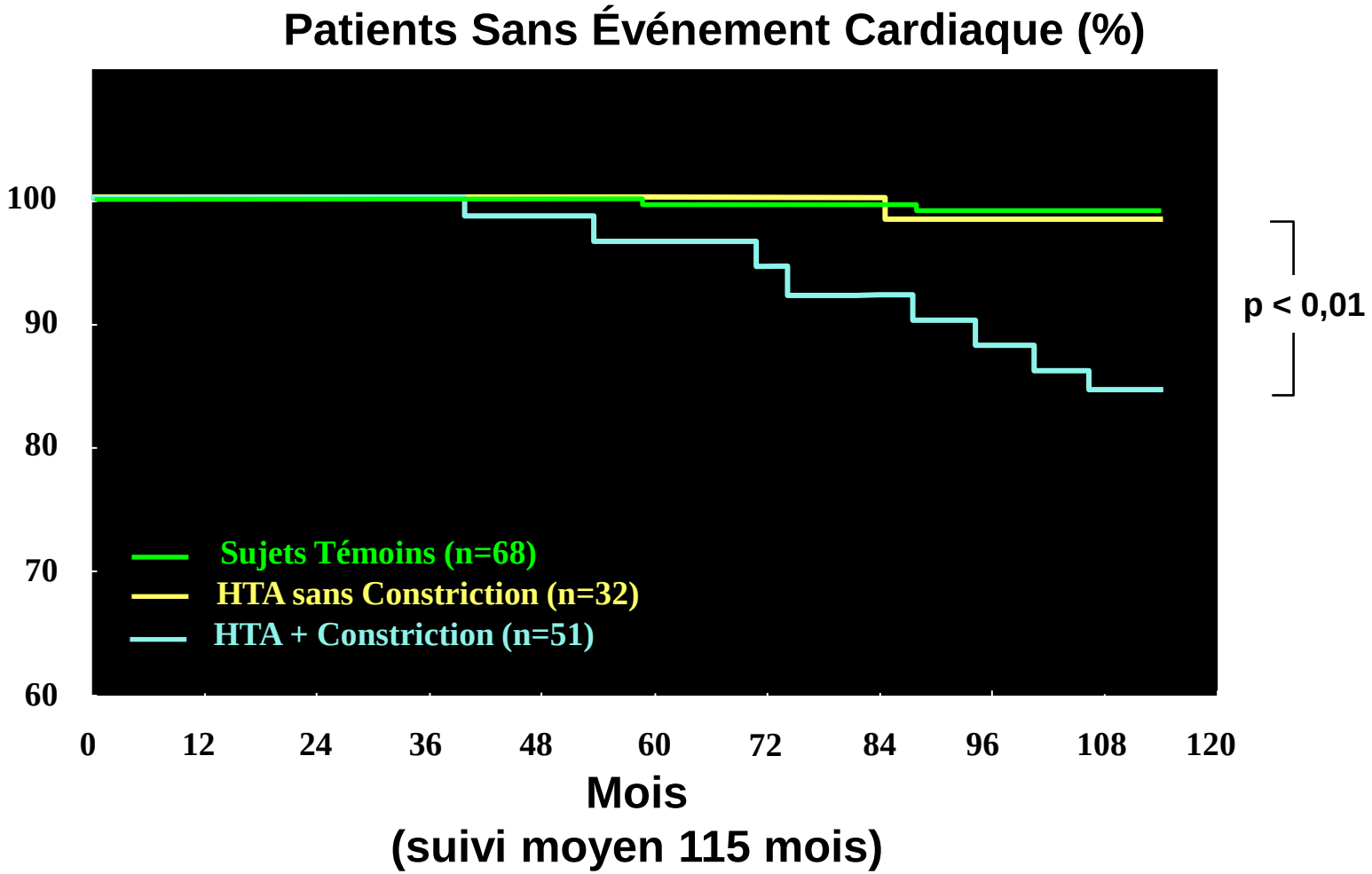
# Dysfonction endothéliale (cold pressor test): IEC atténue la constriction dépendante de l'activité sympathique et l'absence de vasodilatation flux dépendant




… quantitative angiography
And an intracoronary Doppler catheter

Antony et coll. Circulation 1996; 94: 3115-3122.

# Valeur Prédictive de la Dysfonction Endothéliale Coronaire (Test au Froid)
## - Coronaires angiographiquement « normales » -




Nitenberg et coll. Atherosclerosis 2004; 173: 117-125

***Hypertension***

**=> *Anomalies Structurelles et/ou Fonctionnelles***

**1- Artères Coronaires Épicardiques**

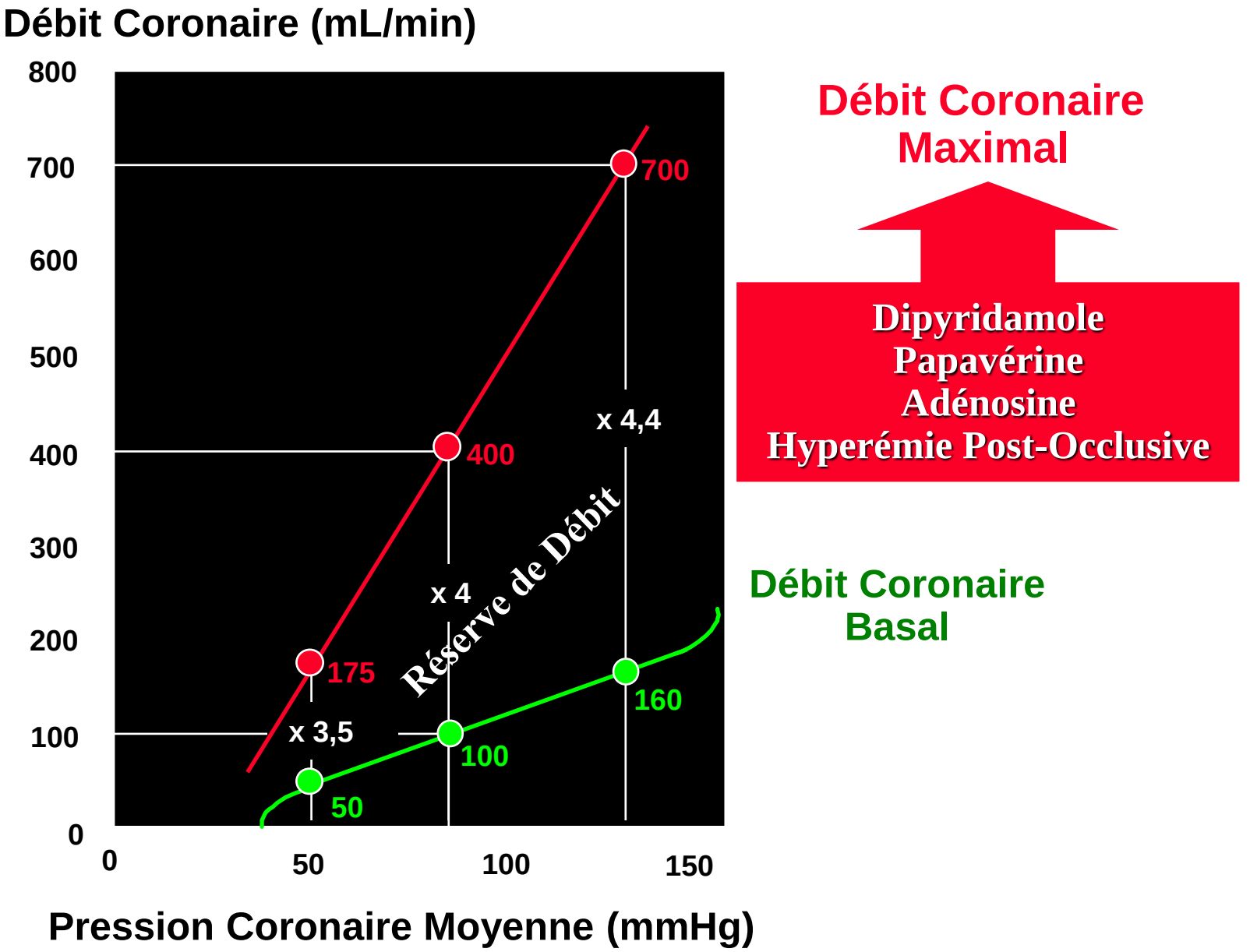
**2- Petites Artères et Artérioles**

**3- Capillaires**

**RESERVE CORONAIRE**

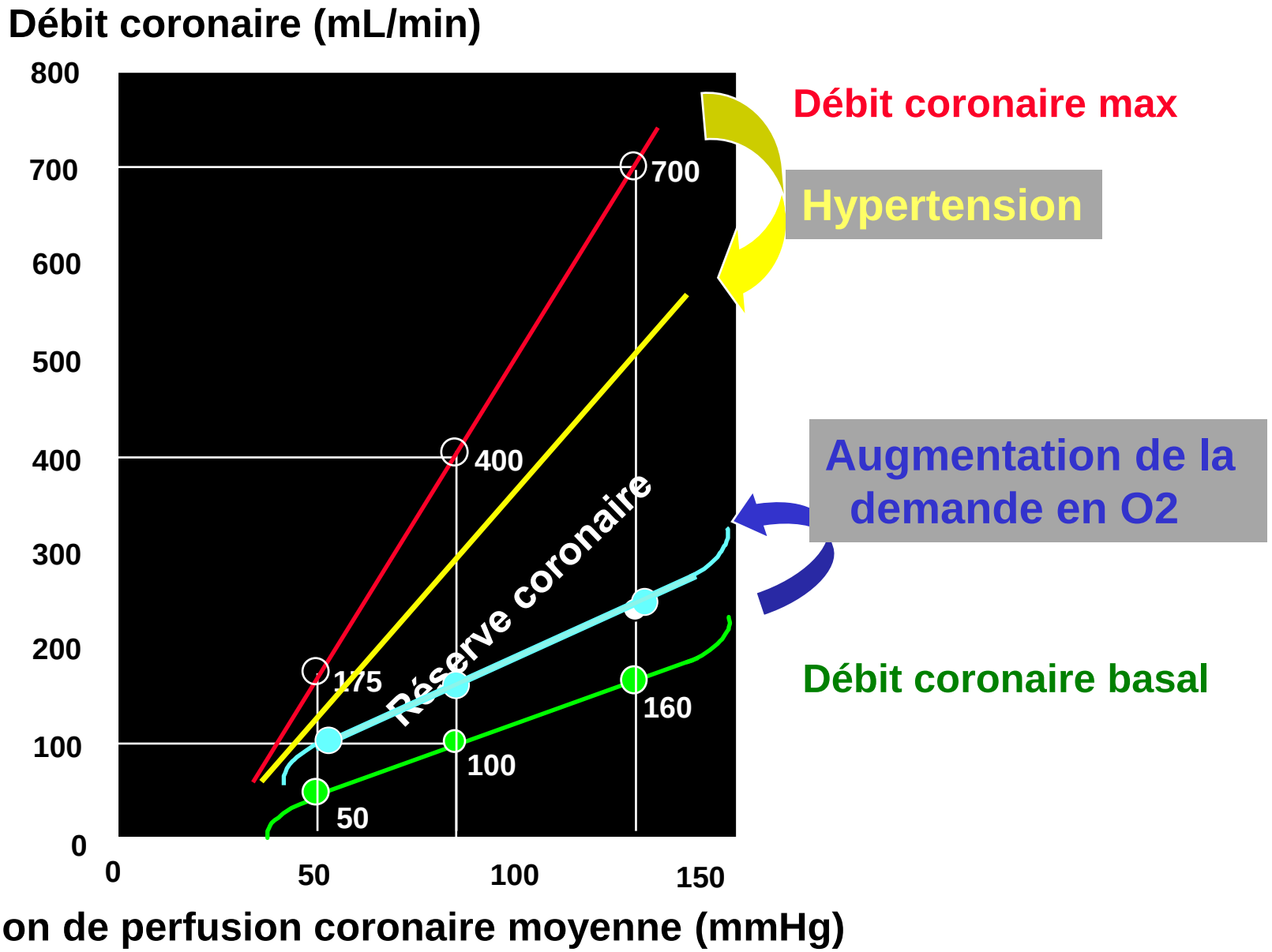
**- pour une pression de perfusion coronaire donnée, le débit basal est autorégulé, entre 50 et 130 mmHg**

**- si on dilate pharmacologiquement les vaisseaux coronaires cette autorégulation disparait et le débit coronaire augmente alors de manière linéaire avec la pression de perfusion**



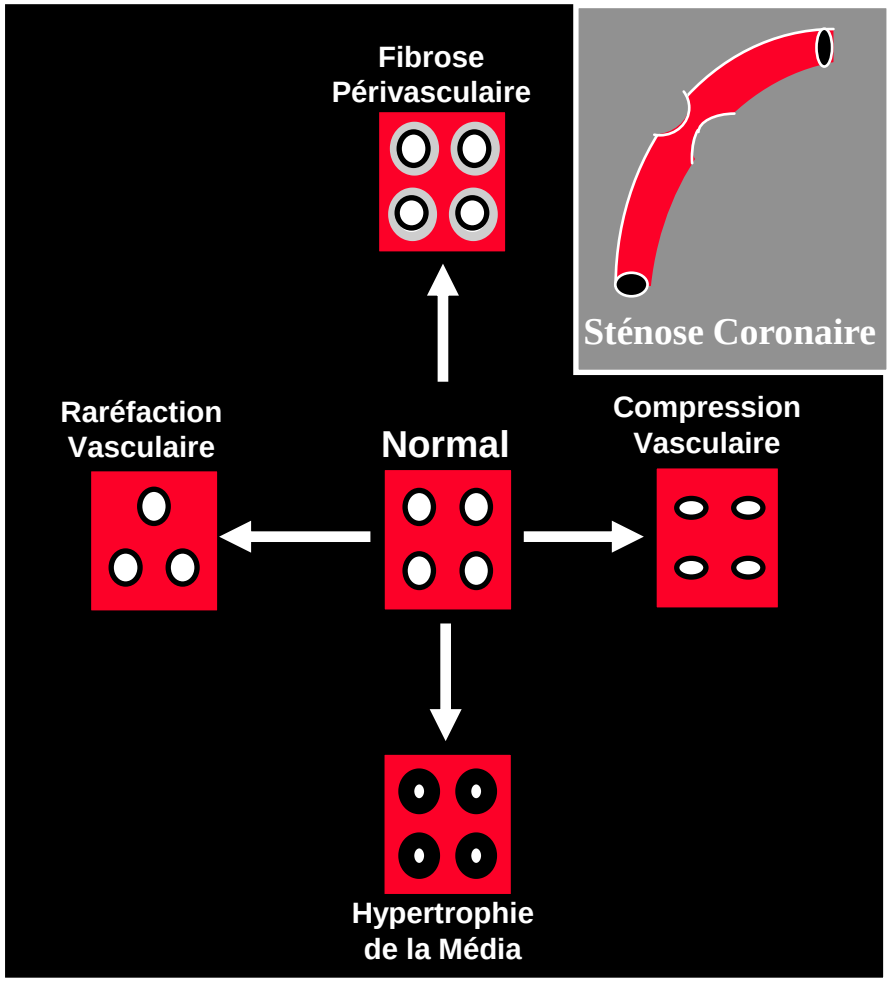

Hoffman Circulation 1984; 70: 153-159.

# Réserve coronaire et hypertension
## Diminution de la surface de section maximale des Coronaires




Hoffman Circulation 1984; 70: 153-159.

# Mécanismes responsables
# de la diminution de la surface de section des artérioles coronaires
# dans l'hypertension artérielle




Alain Nitenberg, mt cardio 2005

***Hypertension***

**=> *Anomalies Structurelles et/ou Fonctionnelles***

**1- Artères Coronaires Épicardiques**

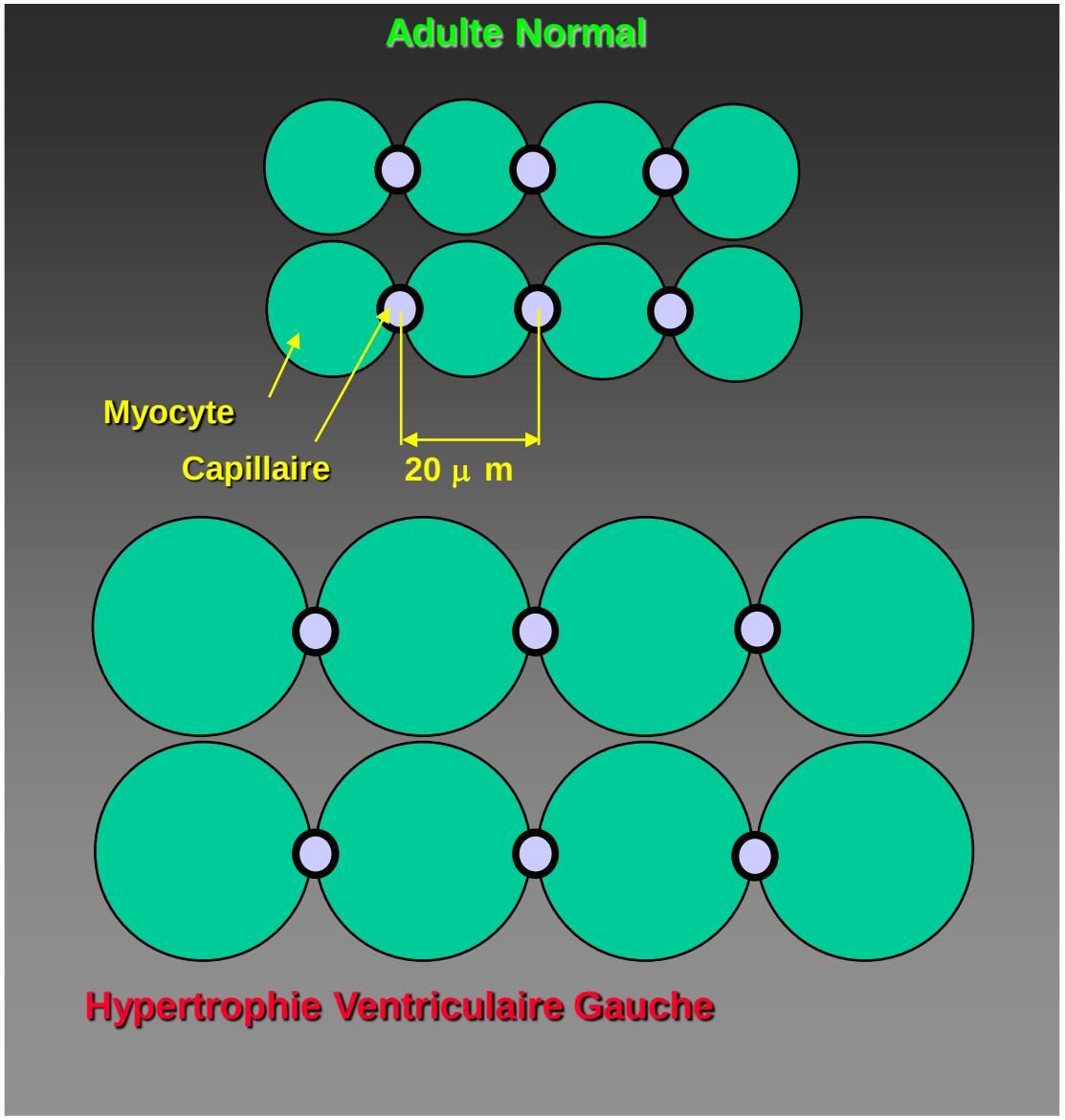
**2- Petites Artères et Artérioles**

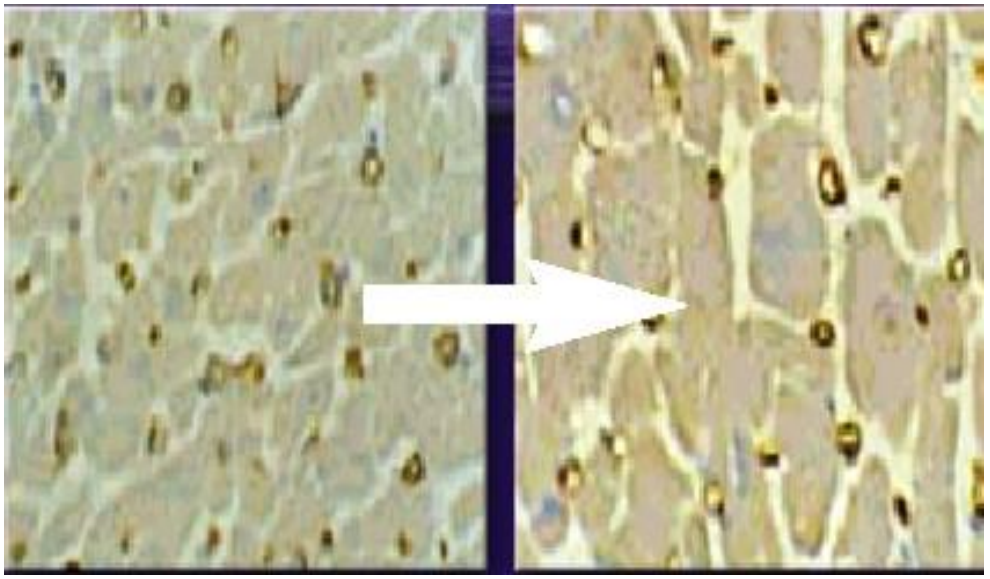
**3- Capillaires**

HTA => Hypertrophie des Myocytes

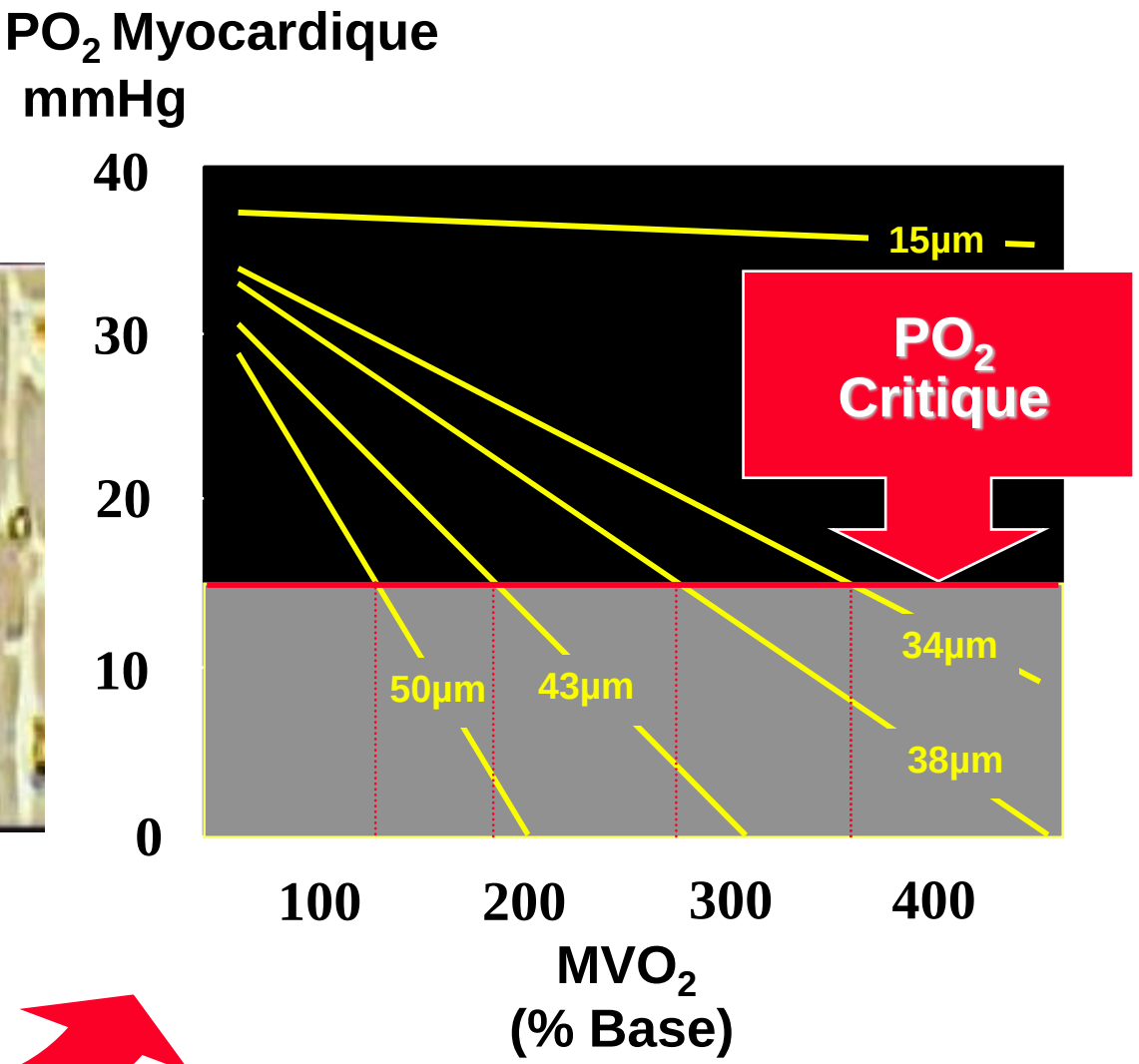
=> Densité Capillaire

=> Distance Intercapillaire





D'après Ito




Myers Honig Am Physiol 1964; 207: 653-660.

## *Hypertension*

## => *Anomalies Structurelles et/ou Fonctionnelles*

**1- Artères Coronaires Épicardiques**

**2- Petites Artères et Artérioles**

**3- Capillaires**

***Hypertension***

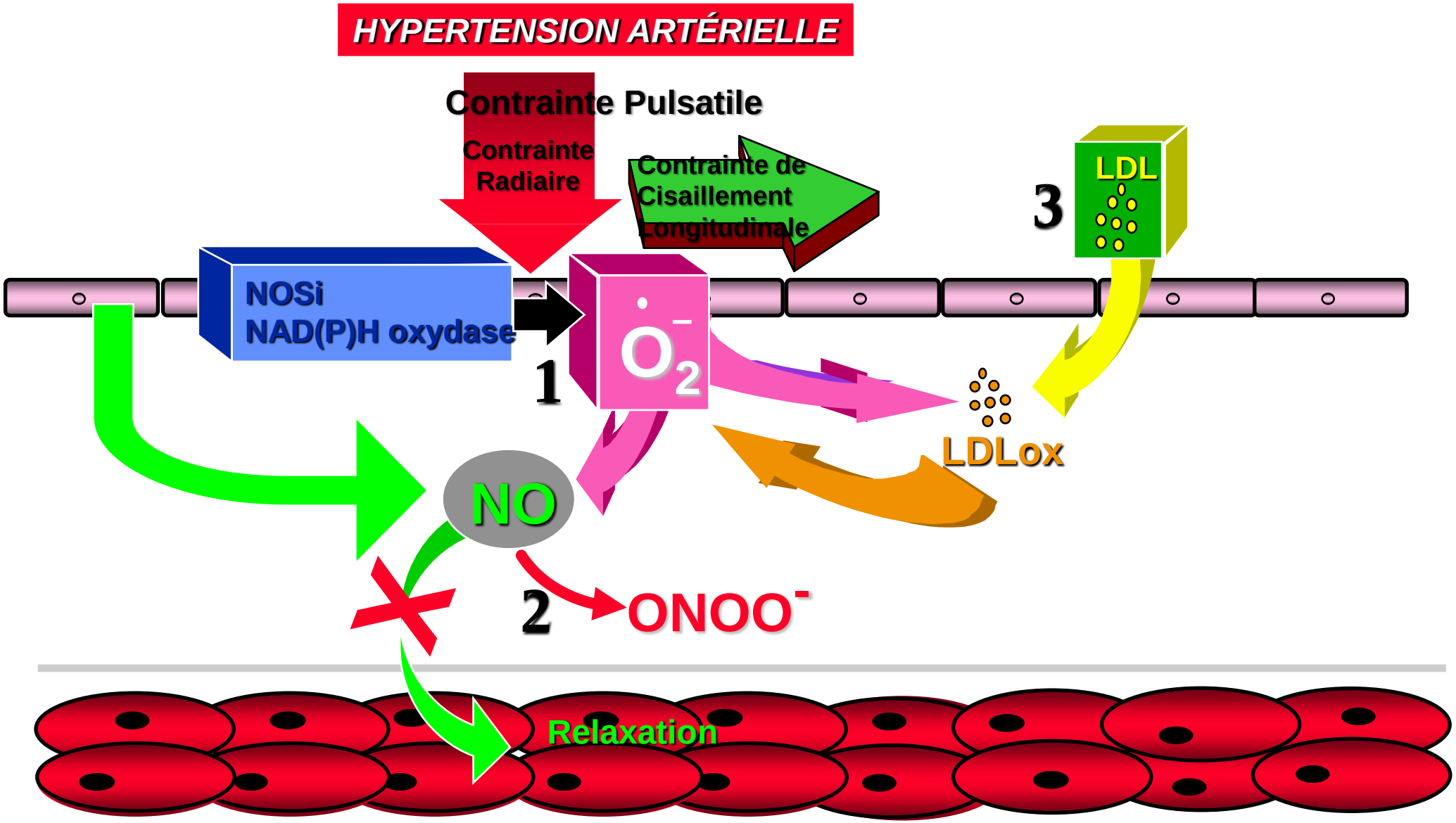
**=> *Anomalies Structurelles et/ou Fonctionnelles***

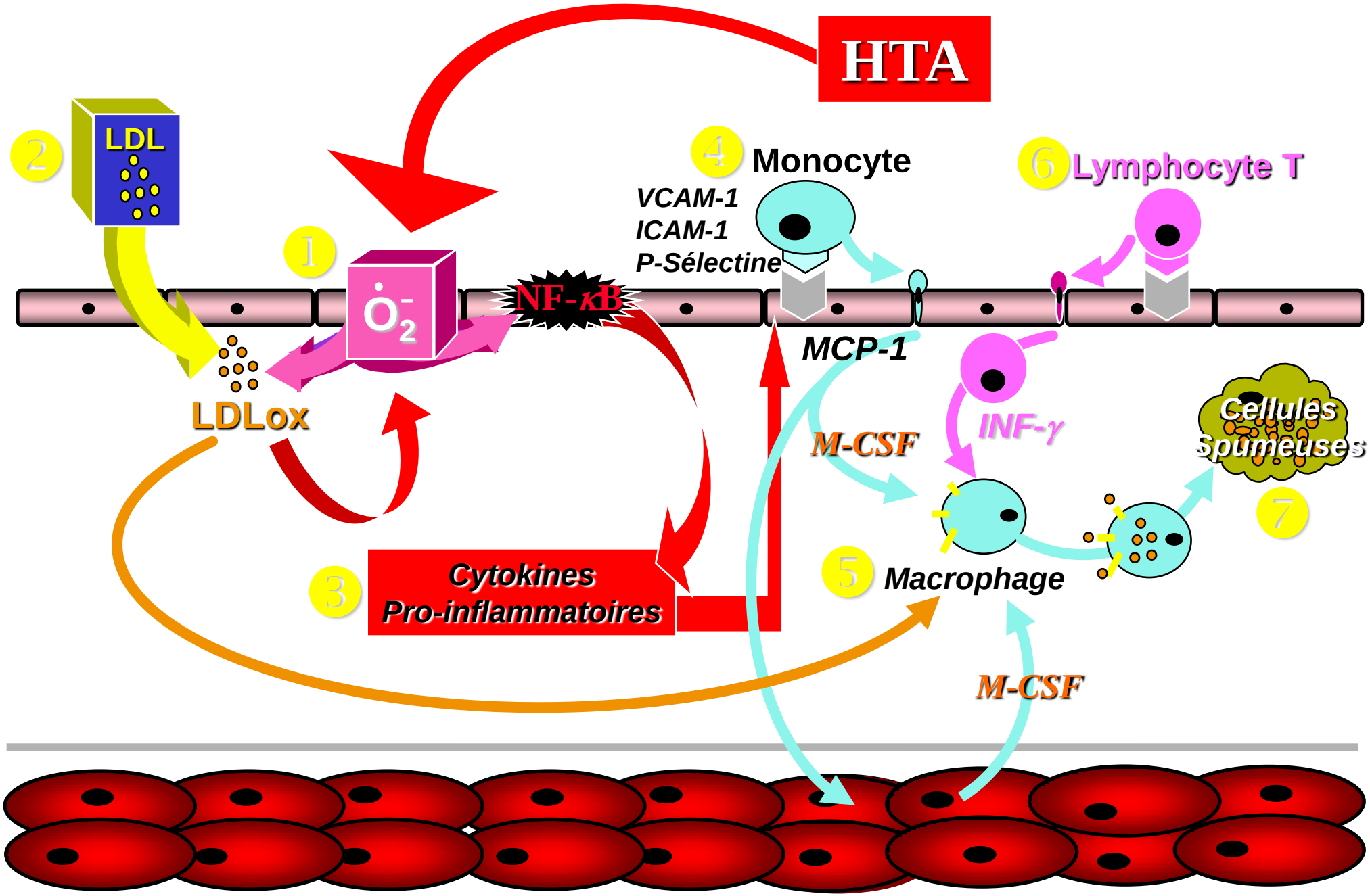
**1- Artères Coronaires Épicardiques**

**2- Petites Artères et Artérioles**

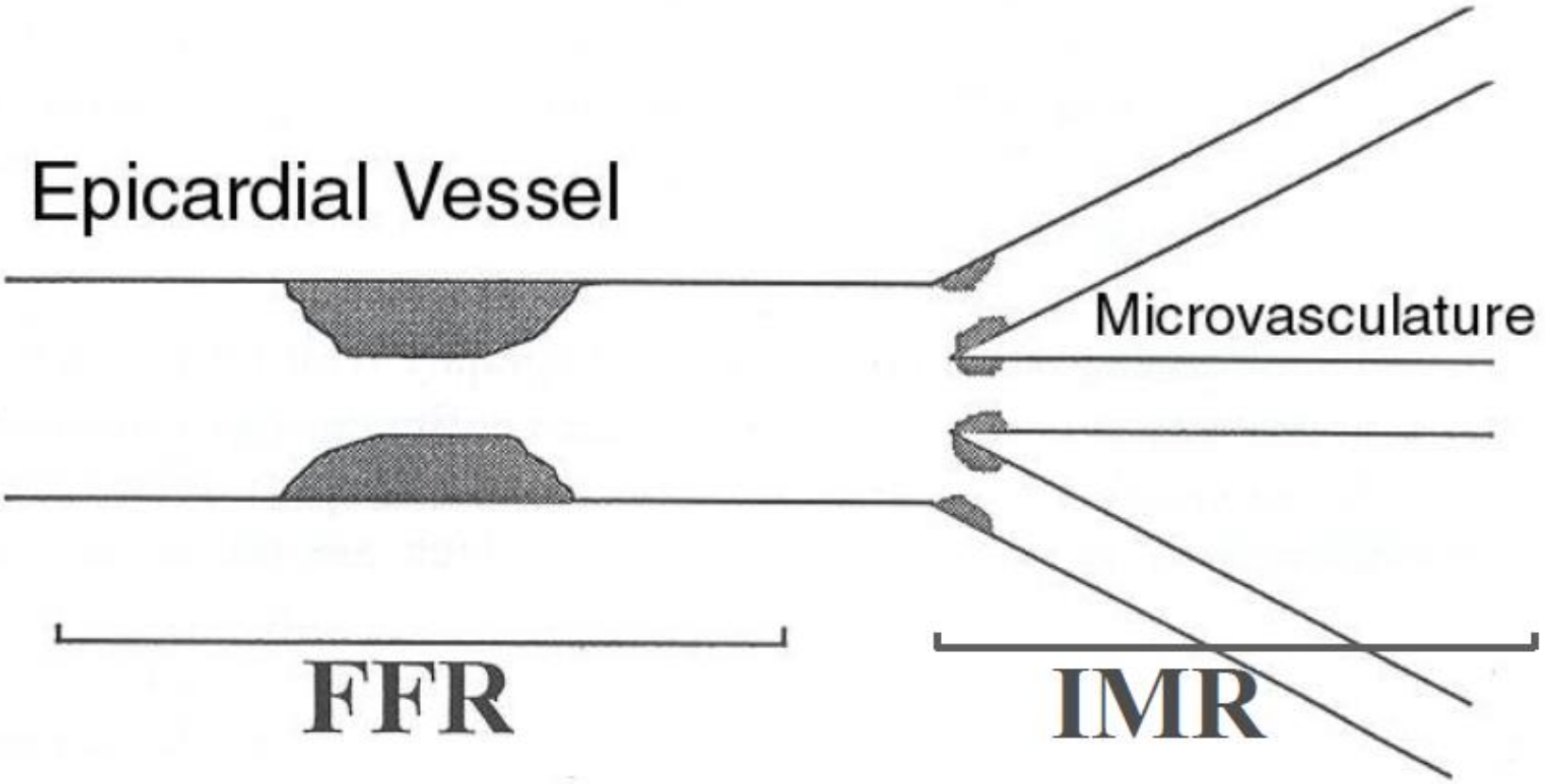
**3- Capillaires**

**=> Athérosclérose coronaire**

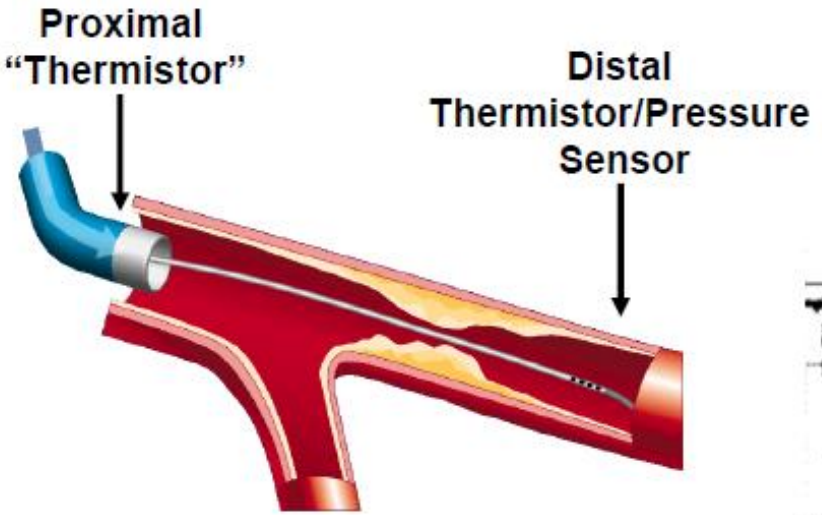

HYPERTENSION ARTÉRIELLE
Contrainte Pulsatile
Contrainte Radiaire
Contrainte de Cisaillement Longitudinale
3
LDL
NOSi
NAD(P)H oxydase
1
$O_2^{\cdot -}$
LDLox
NO
2
$ONOO^-$
Relaxation


HTA
2
LDL
1
$\dot{O}_2^-$
NF-κB
LDLox
4
Monocyte
VCAM-1
ICAM-1
P-Sélectine
MCP-1
6
Lymphocyte T
INF-γ
M-CSF
Cellules spumeuses
7
3
Cytokines Pro-inflammatoires
5
Macrophage
M-CSF

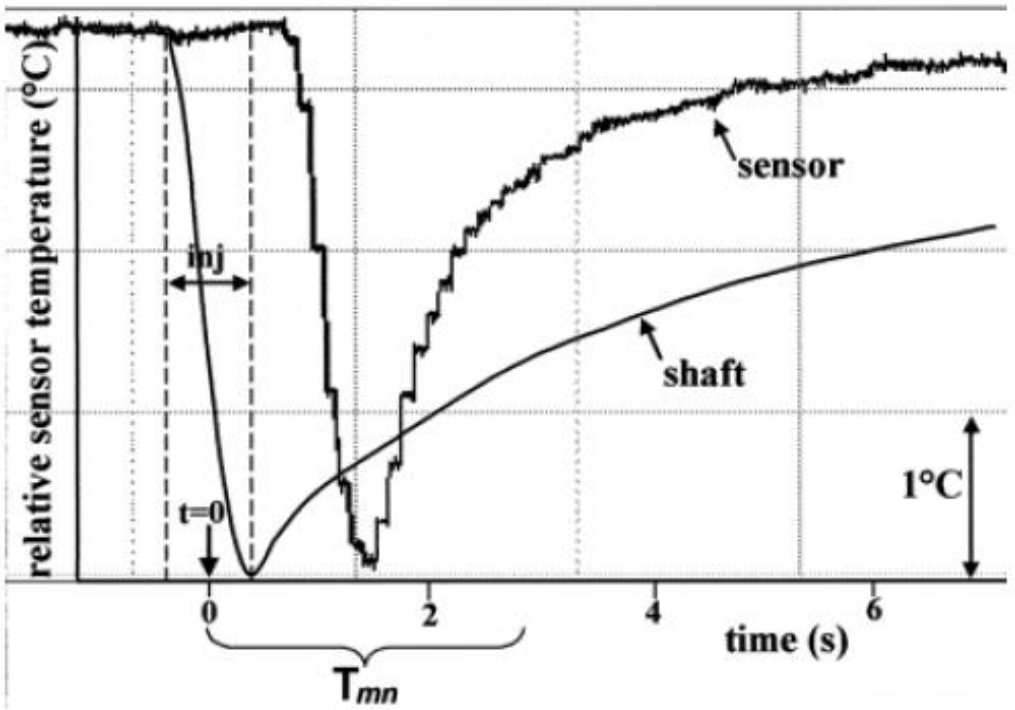
# Index of Microcirculatory Resistance



# Estimation of Coronary Flow




***Calculation of mean transit time***




De Bruyne, et al. Circulation 2002;104:2003

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

ORIGINAL ARTICLE
Ischemic Heart Disease

# Variability of Microcirculatory Resistance Index and Its Relationship With Fractional Flow Reserve in Patients With Intermediate Coronary Artery Lesions

Tadashi Murai, MD; Tetsumin Lee, MD; Taishi Yonetsu, MD; Toshiyuki Iwai, MD;
Takamitsu Takagi, MD; Keiichi Hishikari, MD; Ryo Masuda, MD;

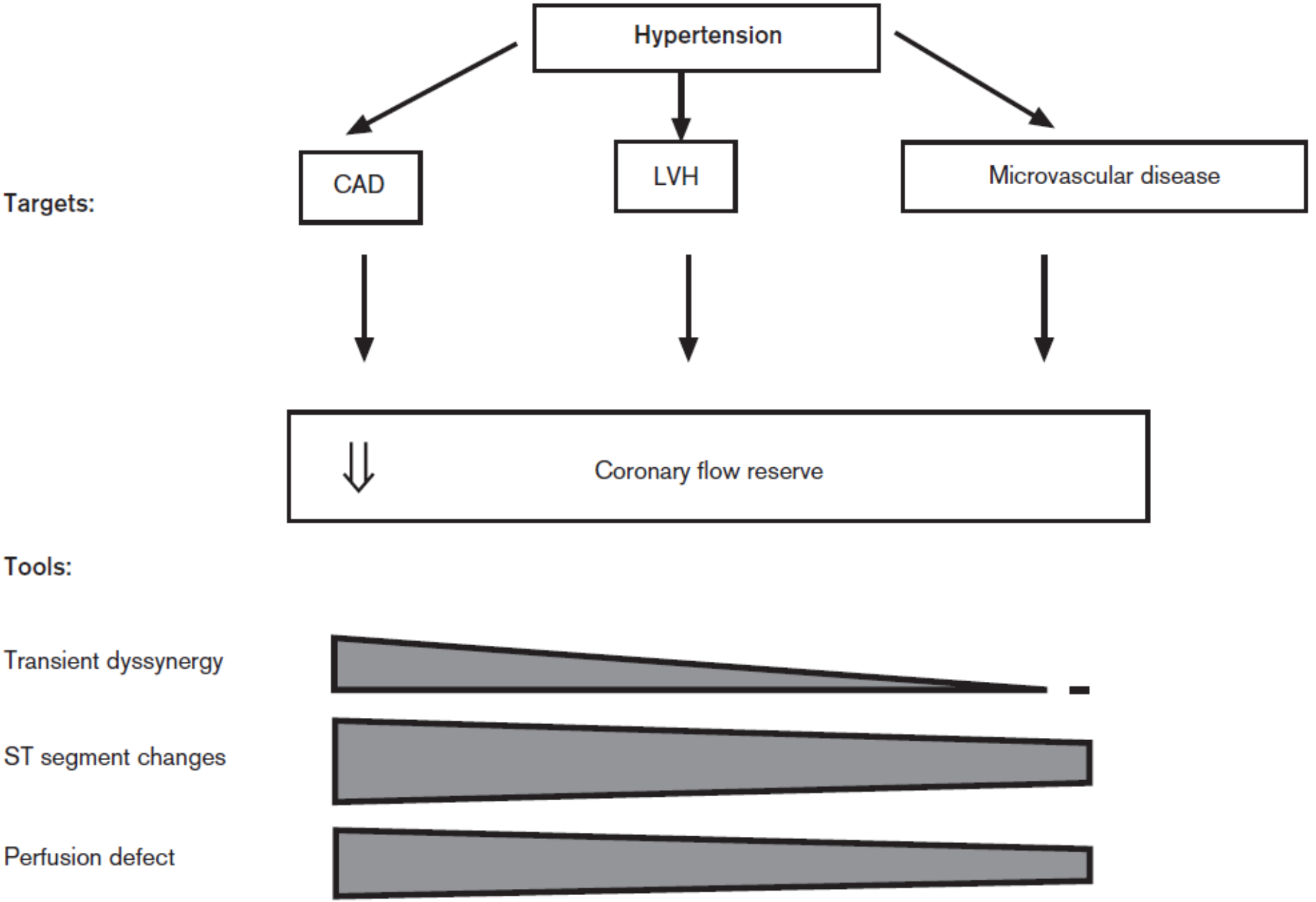
**Chez des patients présentant des sténoses coronaires intermédaires l'existence d'une altération de la microcirculation est fortement associée à l'existence d'une HTA**

cular resistance in patients with intermediate coronary lesions.

| Multivariate logistic regression | | | |
|---|---|---|---|
| Female gender | 1.19 | 0.42–3.38 | 0.74 |
| RCA location | 4.52 | 1.84–11.11 | 0.001 |
| Hypertension | 3.03 | 1.15–7.96 | 0.025 |
| BSA | 0.13 | 0.01–1.72 | 0.12 |

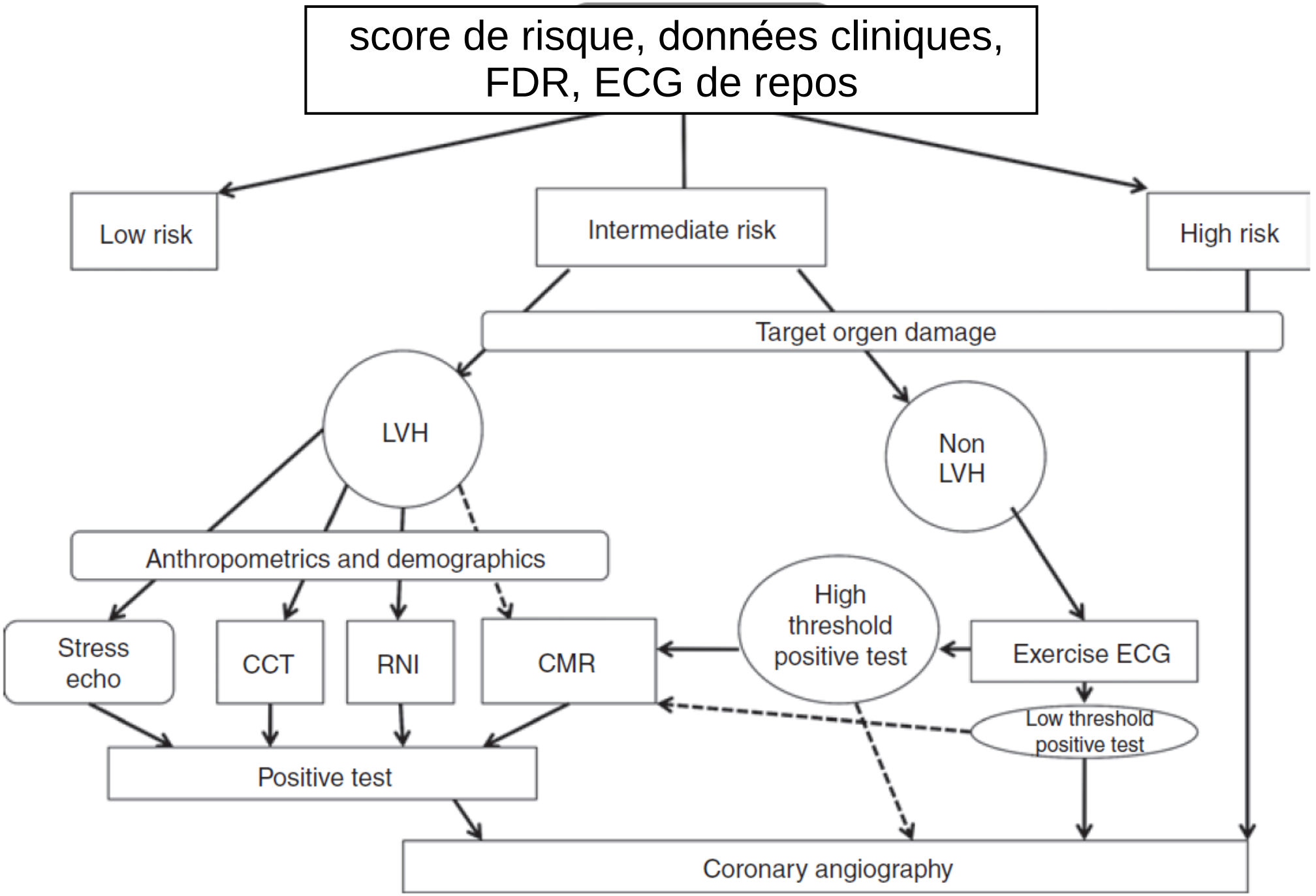
sistance of the perfusion territory. Intermediate coronary lesions may result in increased microcirculatory resistance irrespective of functional significance of the stenosis, with significant regional difference in microvascular resistance. (*Circ J* 2013; **77**: 1769–1776)

# Evaluation du retentissement cardiaque de l'HTA



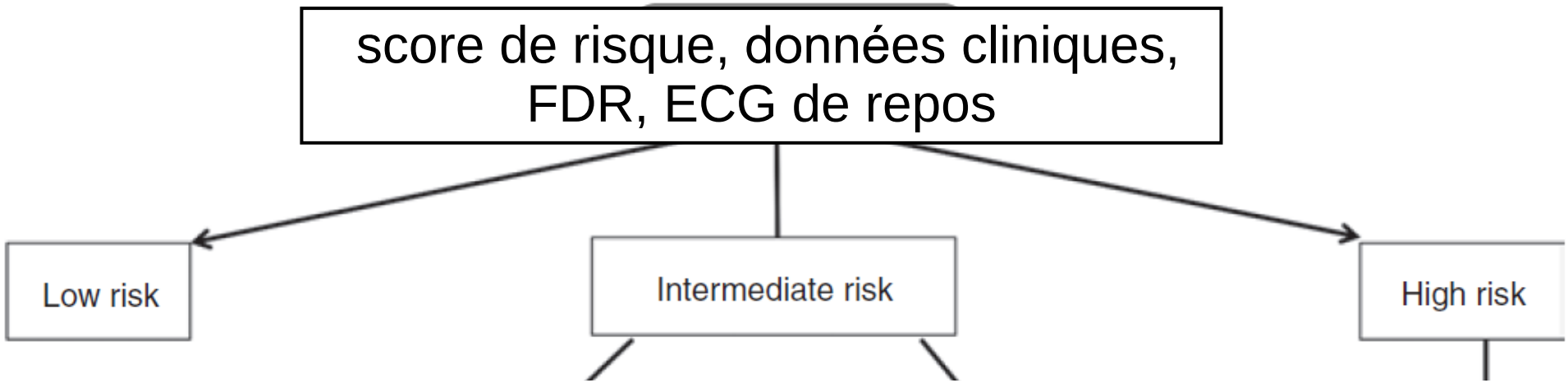

D. Chin. AJH 2012

# Recherche d'une coronaropathie chez un patient hypertendu




D. Chin. AJH 2012

# Clinical tests for the diagnosis of CAD in the hypertensive population




## Approche Bayésienne

La valeur prédictive d'un test diagnostique est directement liée à:

- la sensibilité et à la spécificité du test
- **la probabilité prétest de l'existence de la maladie** (score de risque, données cliniques, FDR, ECG de repos).

L'apport d'un test diagnostique est maximal chez les patients ayant une probabilité prétest intermédiaire de maladie coronarienne.

**Hypertension lowers the specificity of exercise ECG and perfusion scintigraphy.**

**An exercise test, demonstrating a normal aerobic capacity and without significant ECG changes, has an acceptable negative predictive value in patients without strong symptoms indicative of obstructive CHD.**

2013 ESH/ESC Guidelines

# Use of exercise or pharmacologic stress testing in combination with imaging

| Recommendations | Class | Level |
|---|---|---|
| An imaging stress test is recommended as the initial test for diagnosing SCAD if the PTP is between 66–85% or if LVEF is <50% in patients without typical angina. | I | B |
| An imaging stress test is recommended in patients with resting ECG abnormalities which prevent accurate interpretation of ECG changes during stress. | I | B |
| Exercise stress testing is recommended rather than pharmacologic testing whenever possible. | I | C |
| An imaging stress test should be considered in symptomatic patients with prior revascularization (PCI or CABG). | IIa | B |
| An imaging stress test should be considered to assess the functional severity of intermediate lesions on coronary arteriography. | IIa | B |

CABG = coronary artery bypass graft; ECG = electrocardiogram; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; PTP = pre-test probability; SCAD = stable coronary artery disease.
This slide corresponds to Table 15 in the full text.



Eur Heart J 2013;34:2949–3003. doi:10.1093/eurheartj/eht296

# Use of coronary CTA for the diagnosis of SCAD

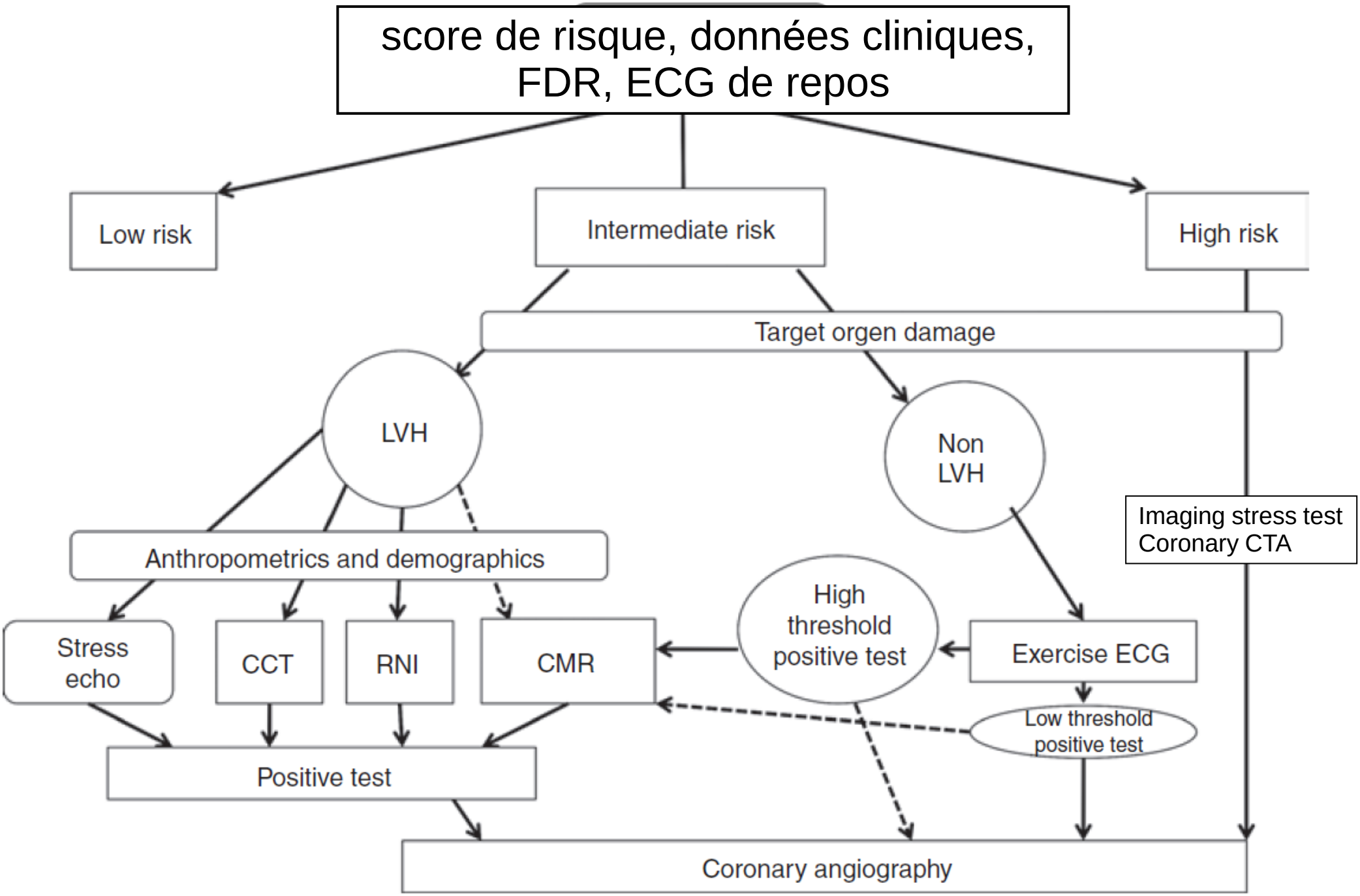
| Recommendations | Class | Level |
|---|---|---|
| Coronary CTA should be considered as an alternative to stress imaging techniques for ruling out SCAD in patients within the lower range of intermediate PTP for SCAD in whom good image quality can be expected. | IIa | C |
| Coronary CTA should be considered in patients within the lower range of intermediate PTP for SCAD after a non-conclusive exercise ECG or stress imaging test or who have contraindications to stress testing in order to avoid otherwise necessary invasive coronary angiography if fully diagnostic image quality of coronary CTA can be expected. | IIa | C |
| Coronary calcium detection by CT is not recommended to identify individuals with coronary artery stenosis. | III | C |
| Coronary CTA is not recommended in patients with prior coronary revascularization. | III | C |
| Coronary CTA is not recommended as a 'screening' test in asymptomatic individuals without clinical suspicion of coronary artery disease. | III | C |

CT = computed tomography; CTA = computed tomography angiography; ECG = electrocardiogram; PTP = pre-test probability; SCAD = stable coronary artery disease.
This slide corresponds to Table 16 in the full text.



Eur Heart J 2013;34:2949–3003. doi:10.1093/eurheartj/eht296

# Clinical tests for the diagnosis of CAD in the hypertensive population




Modifié de D. Chin. AJH 2012

**Table 3** Selected sensitivities and specificities of non-invasive tests for the detection of coronary artery disease as reported in the ACC/AHA 2012 and ESC 2013 guidelines

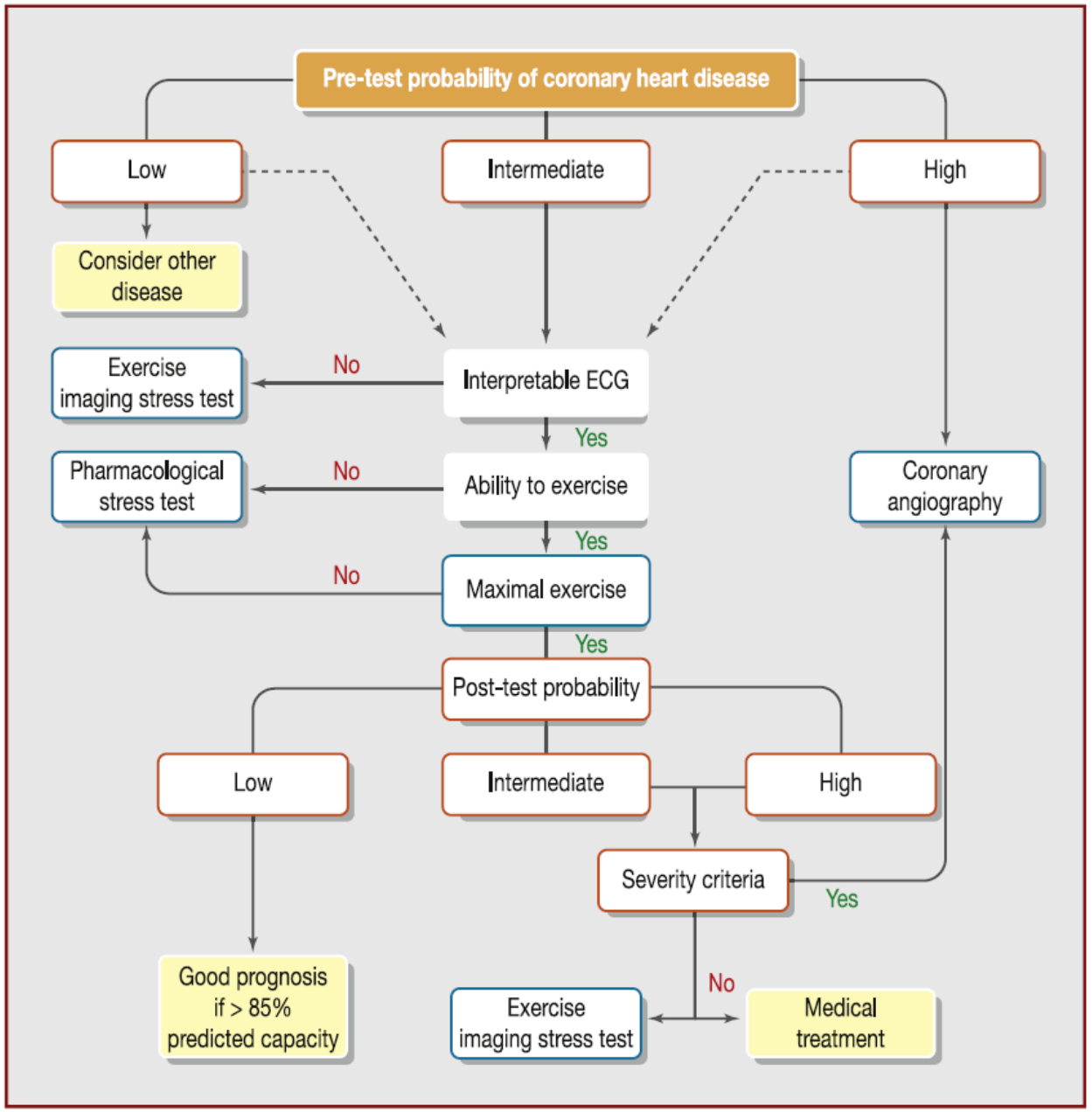
| | Sensitivity | | Specificity | |
|---|---|---|---|---|
| | ACC/AHA 2012 | ESC 2013 | ACC/AHA 2012 | ESC 2013 |
| Exercise ECG | 0.68 | 0.45–0.50 | 0.77 | 0.85–0.90 |
| ECHO | | | | |
| Exercise or pharm | 0.76 | | 0.88 | |
| Exercise | | 0.80–0.85 | | 0.80–0.88 |
| Pharm | | 0.79–0.83 | | 0.82–0.86 |
| SPECT | | | | |
| Exercise or pharm | 0.88 | | 0.77 | |
| Exercise | | 0.73–0.92 | | 0.63–0.87 |
| Pharm | | 0.90–0.91 | | 0.75–0.84 |
| PET | | | | |
| Exercise or pharm | 0.91 | | 0.82 | |
| Pharm PET | | 0.81–0.97 | | 0.74–0.91 |
| CMR | | | | |
| Dobutamine | | 0.79–0.88 | | 0.82–0.86 |
| Vasodilator | | 0.67–0.94 | | 0.61–0.85 |
| CCTA | | 0.95–0.99 | | 0.64–0.93 |

ACC/AHA 2012 estimates adapted from Garber and Solomon.[28] ESC 2013 estimates were collated from multiple studies and adapted from Montalescot *et al*.[7]
ACC, American College of Cardiology; AHA, American Heart Association; CMR, cardiovascular MR; ESC, European Society of Cardiology; PET, positron emission tomography; SPECT, single photon emission CT.

**Fordyce CB, Douglas PS. Heart 2016;102:555–564**

# French Society of Cardiology guidelines on exercise tests (part 2): Indications for exercise tests in cardiac diseases

Archives of Cardiovascular Disease 2018



# 2013 ESH/ESC Guidelines
# Diagnosis of coronary artery disease in the HT population

**When the exercise ECG is positive or uninterpretable/ambiguous, an imaging test of inducible ischaemia is warranted**

**Stress-induced wall motion abnormalities are highly specific for angiographically assessed epicardial coronary artery stenosis,**

**whereas myocardial perfusion abnormalities are frequently found with angiographically normal coronary arteries associated with LVH and/or coronary microvascular disease**

# Hypertension artérielle

**Hypertrophie et remodelage cardiaque et coronaire**
**Fibrose myocardique, fibrose vasculaire et périasculaire**
**Dysfonction Endothéliale**

**Stress oxydatif**

**Athérosclérose coronaire**

**Déséquilibre Demande/Apport en O2**
**Épisodes d'Ischémie Silencieuse**

**Insuffisance Ventriculaire Gauche**

# Quand et avec quels objectifs traité l’HTA chez le coronarien

# Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis

*Dena Ettehad, Connor A Emdin, Amit Kiran, Simon G Anderson, Thomas Callender, Jonathan Emberson, John Chalmers, Anthony Rodgers, Kazem Rahimi*

***Lancet* 2016; 387: 957-67**

## Summary

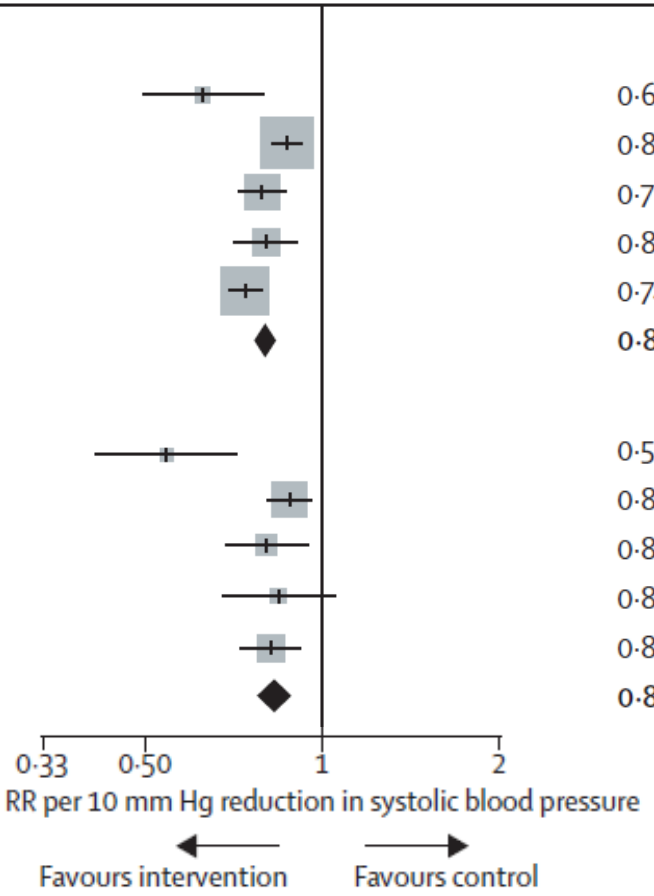
**Background** The benefits of blood pressure lowering treatment for prevention of cardiovascular disease are well established. However, the extent to which these effects differ by baseline blood pressure, presence of comorbidities, or drug class is less clear. We therefore performed a systematic review and meta-analysis to clarify these differences.

**Method** For this systematic review and meta-analysis, we searched MEDLINE for large-scale blood pressure lowering trials, published between Jan 1, 1966, and July 7, 2015, and we searched the medical literature to identify trials up to Nov 9, 2015. All randomised controlled trials of blood pressure lowering treatment were eligible for inclusion if they included a minimum of 1000 patient-years of follow-up in each study arm. No trials were excluded because of presence of baseline comorbidities, and trials of antihypertensive drugs for indications other than hypertension were eligible. We extracted summary-level data about study characteristics and the outcomes of major cardiovascular disease events, coronary heart disease, stroke, heart failure, renal failure, and all-cause mortality. We used inverse variance weighted fixed-effects meta-analyses to pool the estimates.

**Results** We identified 123 studies with 613 815 participants for the tabular meta-analysis. Meta-regression analyses showed relative risk reductions proportional to the magnitude of the blood pressure reductions achieved. Every 10 mm Hg reduction in systolic blood pressure significantly reduced the risk of major cardiovascular disease events (relative risk [RR] 0·80, 95% CI 0·77–0·83), coronary heart disease (0·83, 0·78–0·88), stroke (0·73, 0·68–0·77), and heart failure (0·72, 0·67–0·78), which, in the populations studied, led to a significant 13% reduction in all-cause mortality (0·87, 0·84–0·91). However, the effect on renal failure was not significant (0·95, 0·84–1·07). Similar proportional risk reductions (per 10 mm Hg lower systolic blood pressure) were noted in trials with higher mean baseline systolic blood pressure and trials with lower mean baseline systolic blood pressure (all $p_{trend}>0·05$). There was no clear evidence that proportional risk reductions in major cardiovascular disease differed by baseline disease history, except for diabetes and chronic kidney disease, for which smaller, but significant, risk reductions were detected. β blockers were inferior to other drugs for the prevention of major cardiovascular disease events, stroke, and renal failure. Calcium channel blockers were superior to other drugs for the prevention of stroke. For the prevention of heart failure, calcium channel blockers were inferior and diuretics were superior to other drug classes. Risk of bias was judged to be low for 113 trials and unclear for 10 trials. Heterogeneity for outcomes was low to moderate; the $I^2$ statistic for heterogeneity for major cardiovascular disease events was 41%, for coronary heart disease 25%, for stroke 26%, for heart failure 37%, for renal failure 28%, and for all-cause mortality 35%.

# Standardised effects of a 10 mm Hg reduction in systolic blood pressure stratified by blood pressure

| | Studies | Intervention | | Control | | RR (95% CI) per 10 mmHg Reduction in SBP | P trend |
|---|---|---|---|---|---|---|---|
| | | Events | Participants | Events | Participants | | |
| **Major cardiovascular events** | | | | | | | 0·22 |
| <130 | 4 | 542 | 4547 | 530 | 3881 | 0·63 (0·50–0·80) | |
| 130–139 | 17 | 5375 | 47103 | 5856 | 47167 | 0·87 (0·82–0·92) | |
| 140–149 | 7 | 4365 | 33333 | 4694 | 33062 | 0·79 (0·72–0·87) | |
| 150–159 | 13 | 1289 | 21290 | 1257 | 20088 | 0·80 (0·71–0·91) | |
| ≥160 | 14 | 1638 | 31045 | 1731 | 24060 | 0·74 (0·69–0·79) | |
| **Total** | | | | | | **0·80 (0·77–0·83)** | |
| **Coronary heart disease** | | | | | | | 0·93 |
| <130 | 5 | 489 | 6071 | 620 | 5395 | 0·55 (0·42–0·72) | |
| 130–139 | 18 | 2258 | 47608 | 2461 | 47670 | 0·88 (0·80–0·96) | |
| 140–149 | 8 | 1225 | 34834 | 1307 | 34581 | 0·80 (0·69–0·94) | |
| 150–159 | 12 | 409 | 20386 | 442 | 19788 | 0·84 (0·68–1·05) | |
| ≥160 | 13 | 481 | 28086 | 471 | 21113 | 0·82 (0·73–0·92) | |
| **Total** | | | | | | **0·83 (0·78–0·88)** | |

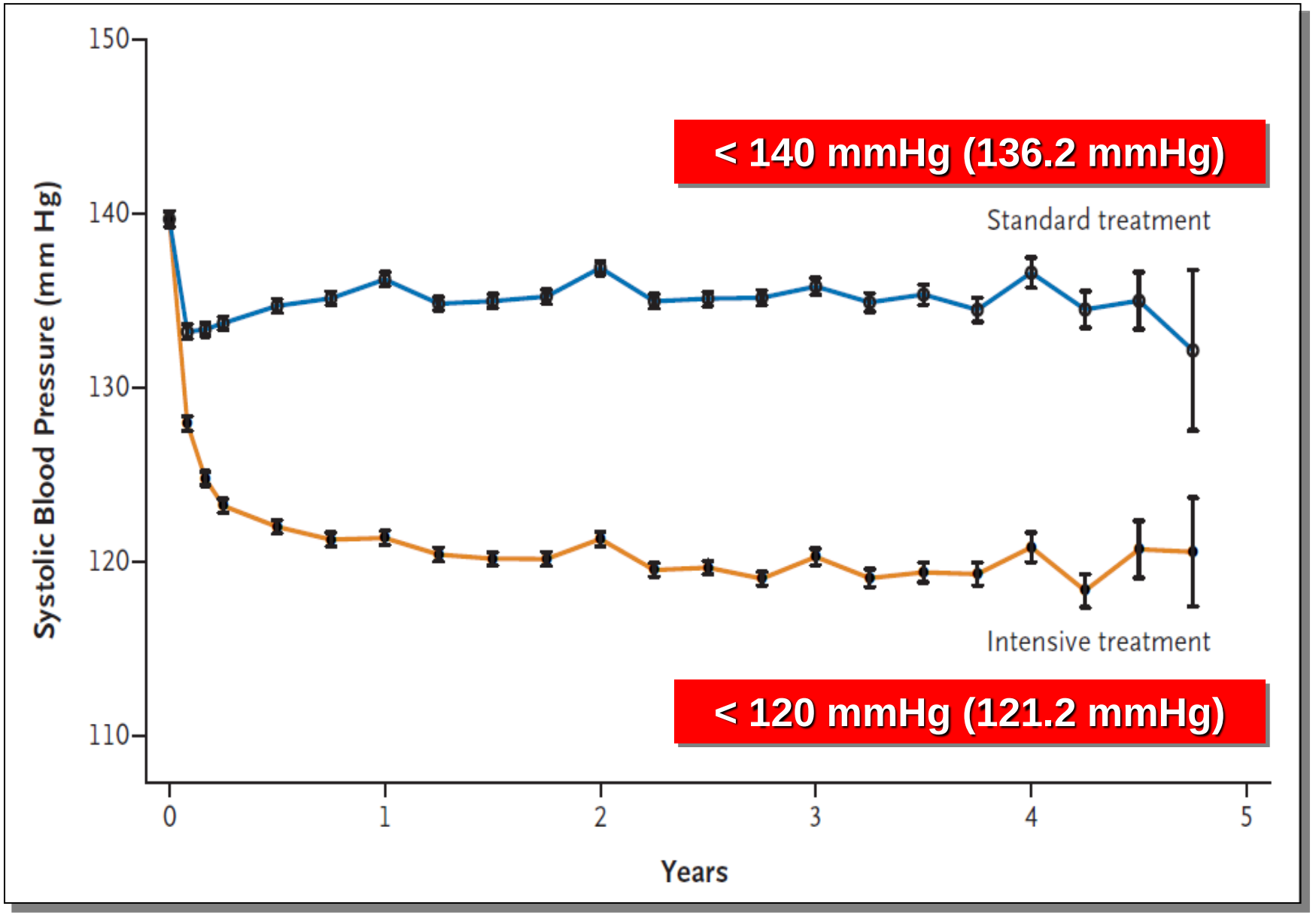



**A 10 mm Hg reduction in systolic blood pressure reduced the risk of major cardiovascular disease events by 20%, coronary heart disease by 17%, stroke by 27%, heart failure by 28%, and all-cause mortality by 13%.**

**Similar proportional risk reductions (per 10 mm Hg lower SBP) were noted in trials with higher mean baseline SBP and trials with lower mean baseline SBP (<130 mmHg)**

*Dena Ettehad et al. Lancet* 2016; 387: 957-67

# Optimal Blood Pressure Targets in the SPRINT Study




*SPRINT Research Group. N Eng J Med 2015; 373: 2103-2116*

# Cardiovascular event rates and mortality according to achieved systolic and diastolic blood pressure in patients with stable coronary artery disease: an international cohort study

*Emmanuelle Vidal-Petiot, Ian Ford, Nicola Greenlaw, Roberto Ferrari, Kim M Fox, Jean-Claude Tardif, Michal Tendera, Luigi Tavazzi, Deepak L Bhatt, Philippe Gabriel Steg, for the CLARIFY Investigators**

*Lancet* 2016; 388: 2142–52

Published Online August 30, 2016 http://dx.doi.org/10.1016/S0140-6736(16)31326-5

See Comment page 2061

*Investigators listed in the appendix

**Cardiology and Physiology Departments, Département Hospitalo-Universitaire FIRE, Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, and Paris Diderot University, Sorbonne Paris Cité, Paris, France** (E Vidal-Petiot MD, Prof P G Steg MD); **University of Glasgow, Glasgow, UK** (Prof I Ford PhD, N Greenlaw MSc); **Maria Cecilia Hospital, GVM Care & Research, ES Health Science Foundation, Cotignola, Italy** (Prof R Ferrari MD, Prof L Tavazzi MD); **Department**

## Summary

**Background** The optimum blood pressure target in hypertension remains debated, especially in coronary artery disease, given concerns for reduced myocardial perfusion if diastolic blood pressure is too low. We aimed to study the association between achieved blood pressure and cardiovascular outcomes in patients with coronary artery disease and hypertension.

**Methods** We analysed data from 22 672 patients with stable coronary artery disease enrolled (from Nov 26, 2009, to June 30, 2010) in the CLARIFY registry (including patients from 45 countries) and treated for hypertension. Systolic and diastolic blood pressures before each event were averaged and categorised into 10 mm Hg increments. The primary outcome was the composite of cardiovascular death, myocardial infarction, or stroke. Hazard ratios (HRs) were estimated with multivariable adjusted Cox proportional hazards models, using the 120–129 mm Hg systolic blood pressure and 70–79 mm Hg diastolic blood pressure subgroups as reference.

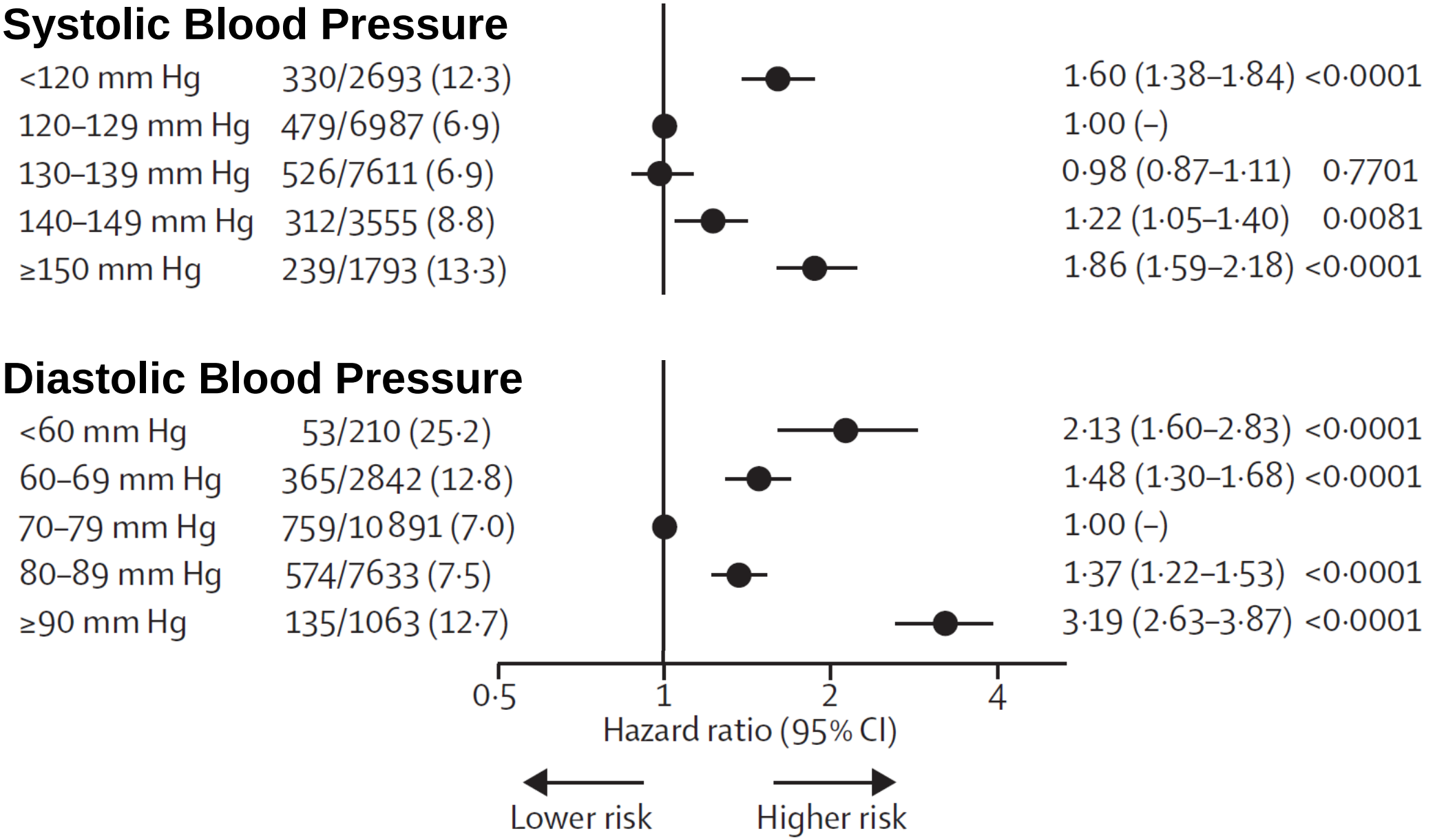
**Findings** After a median follow-up of 5·0 years, increased systolic blood pressure of 140 mm Hg or more and diastolic blood pressure of 80 mm Hg or more were each associated with increased risk of cardiovascular events. Systolic blood pressure of less than 120 mm Hg was also associated with increased risk for the primary outcome (adjusted HR 1·56, 95% CI 1·36–1·81). Likewise, diastolic blood pressure of less than 70 mm Hg was associated with an increase in the primary outcome (adjusted HR 1·41 [1·24–1·61] for diastolic blood pressure of 60–69 mm Hg and 2·01 [1·50–2·70] for diastolic blood pressure of less than 60 mm Hg).

**Interpretation** In patients with hypertension and coronary artery disease from routine clinical practice, systolic blood

| | Number of patients | Mean systolic blood pressure categories | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Total population (n=22 672) | <120 mm Hg (n=2693) | 120–129 mm Hg (n=6946) | 130–139 mm Hg (n=7586) | 140–149 mm Hg (n=3584) | ≥150 mm Hg (n=1863) | p value |
| Age (years) | 22 666 | 65·2 (10·0) | 63·9 (10·4) | 64·3 (10·2) | 65·4 (9·8) | 66·2 (9·6) | 67·21 (9·8) | <0·0001 |
| Men | 22 672 | 17 019 (75%) | 2104 (78%) | 5399 (78%) | 5677 (75%) | 2578 (72%) | 1261 (68%) | <0·0001 |
| Body-mass index (kg/m²) | 22 654 | 27·7 (25·2–30·9) | 26·7 (24·2–29·7) | 27·5 (25·1–30·5) | 27·9 (25·3–31·1) | 28·4 (25·6–31·5) | 28·4 (25·5–31·9) | <0·0001 |
| Diabetes | 22 670 | 7591 (33%) | 835 (31%) | 2160 (31%) | 2545 (34%) | 1306 (36%) | 745 (40%) | <0·0001 |
| Smoking status | | | | | | | | |
| Current | 22 672 | 2569 (11%) | 352 (13%) | 780 (11%) | 861 (11%) | 383 (11%) | 193 (10%) | <0·0001 |
| Former | .. | 10 158 (45%) | 1254 (47%) | 3222 (46%) | 3325 (44%) | 1553 (43%) | 804 (43%) | .. |
| Never | .. | 9945 (44%) | 1087 (40%) | 2944 (42%) | 3400 (45%) | 1648 (46%) | 866 (46%) | .. |
| Systolic blood pressure (mm Hg) | 22 659 | 133·7 (16·7) | 114·3 (10·7) | 125·9 (10·3) | 135·8 (11·3) | 145·5 (13·4) | 159·3 (16·4) | .. |
| Diastolic blood pressure (mm Hg) | 22 659 | 78·2 (10·1) | 71·0 (8·8) | 76·0 (8·4) | 79·2 (9·2) | 82·2 (10·3) | 85·5 (11·7) | .. |
| Heart rate (beats per min) | 22 660 | 68·5 (10·6) | 67·4 (10·2) | 67·9 (10·2) | 68·7 (10·6) | 69·4 (11·1) | 69·6 (11·7) | <0·0001 |
| Myocardial infarction | 22 670 | 13 258 (58%) | 1789 (66%) | 4165 (60%) | 4298 (57%) | 2017 (56%) | 989 (53%) | <0·0001 |
| Percutaneous coronary intervention | 22 670 | 12 962 (57%) | 1632 (61%) | 4106 (59%) | 4282 (56%) | 1962 (55%) | 980 (53%) | <0·0001 |
| Coronary artery bypass graft surgery | 22 670 | 5691 (25%) | 676 (25%) | 1658 (24%) | 1894 (25%) | 939 (26%) | 524 (28%) | 0·0019 |
| Transient ischaemic attack | 22 670 | 801 (4%) | 74 (3%) | 235 (3%) | 277 (4%) | 137 (4%) | 78 (4%) | 0·0652 |
| Stroke | 22 670 | 1089 (5%) | 125 (5%) | 327 (5%) | 341 (4%) | 181 (5%) | 115 (6%) | 0·0407 |
| Hospital admission for heart failure | 22 670 | 1211 (5%) | 219 (8%) | 317 (5%) | 364 (5%) | 193 (5%) | 118 (6%) | <0·0001 |
| Symptoms of heart failure | | | | | | | | |
| None | 22 671 | 18 787 (83%) | 2201 (82%) | 5813 (84%) | 6318 (83%) | 2923 (82%) | 1532 (82%) | 0·0033 |

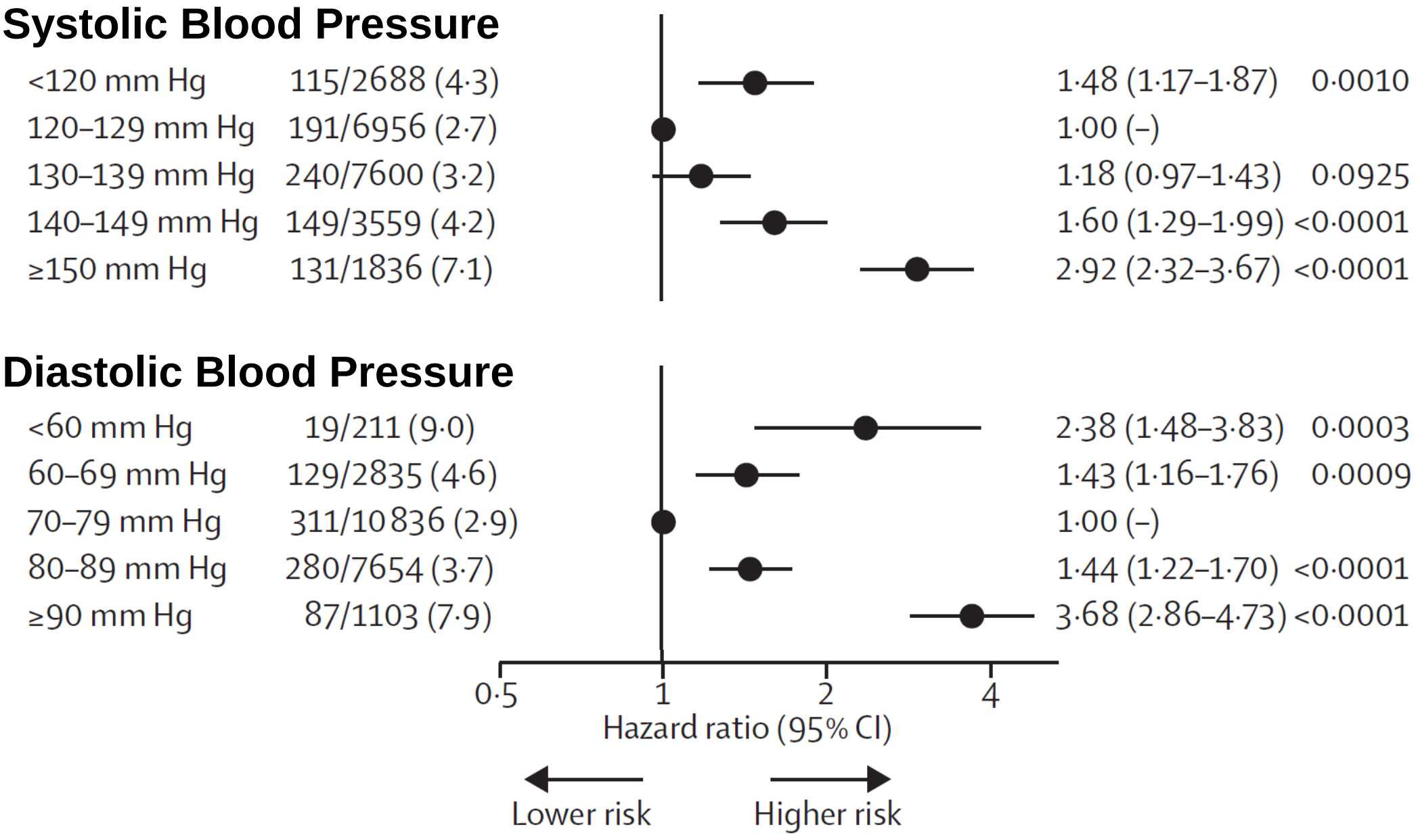
*CLARIFY - Lancet 2016; 388: 2142–52*

# All-cause death by Subgroups of Systolic or Diastolic BP



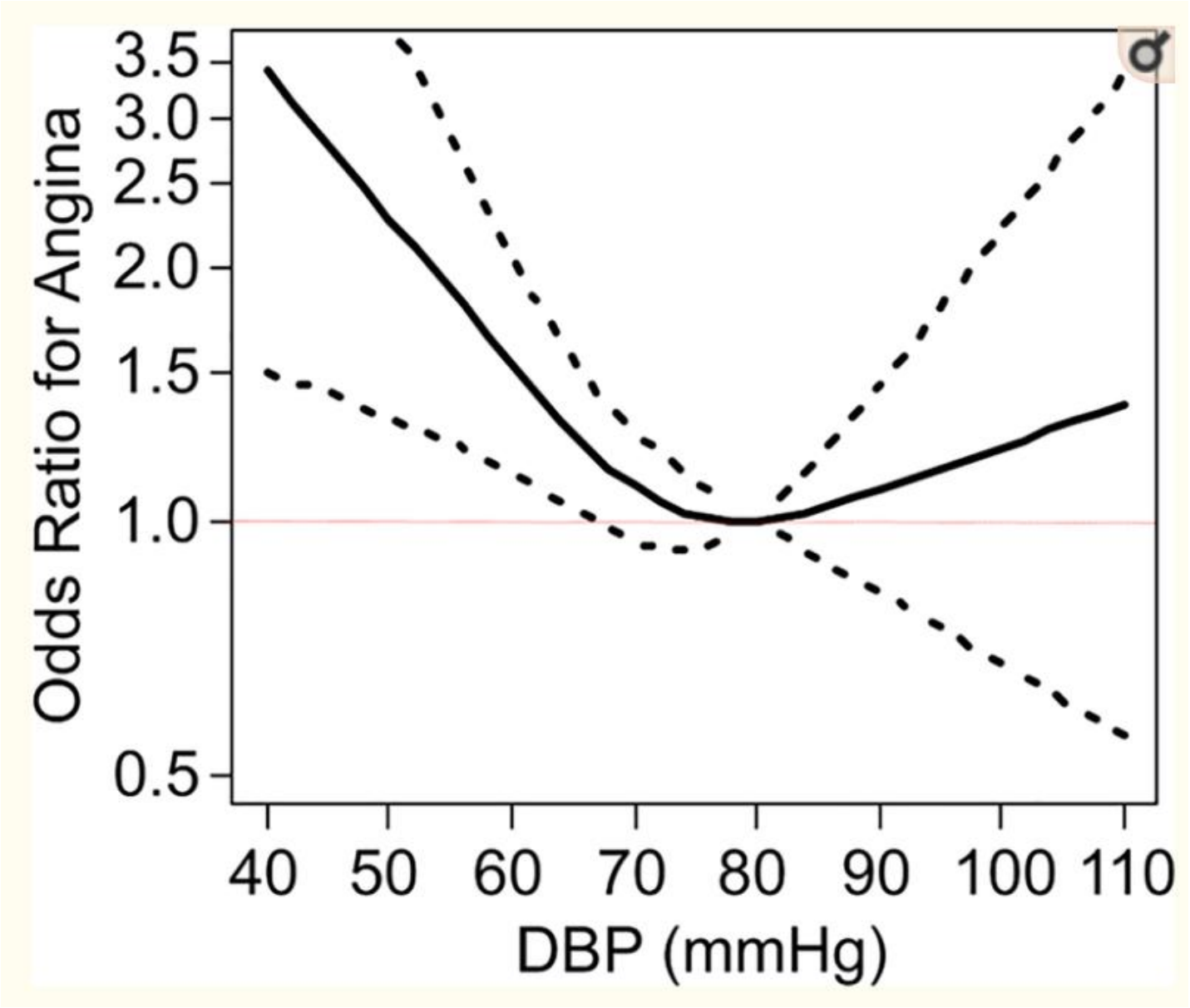

*CLARIFY - Lancet 2016; 388: 2142–52*

# Myocardial Infarction by Subgroups of Systolic or Diastolic BP




*CLARIFY - Lancet 2016; 388: 2142–52*

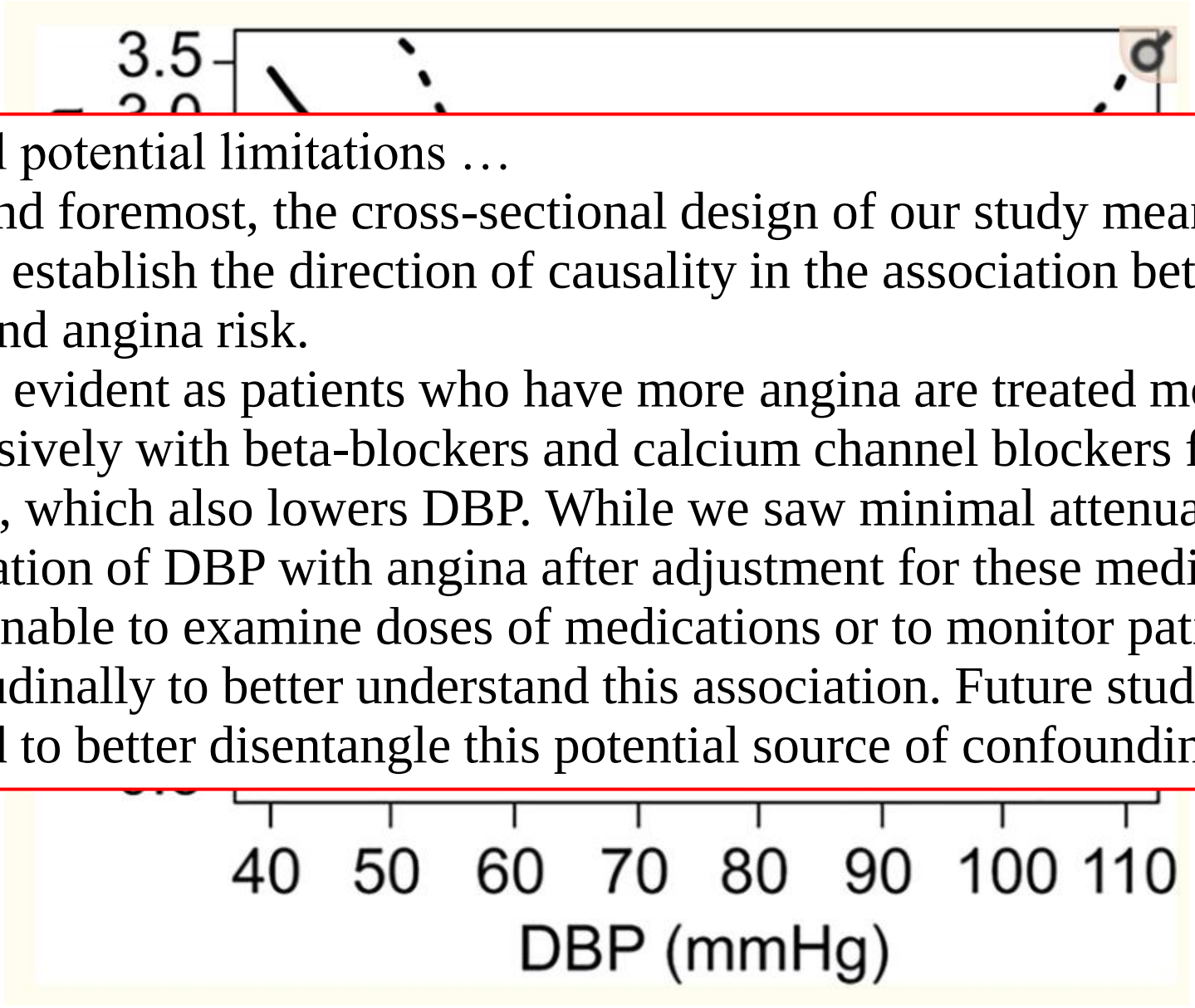
# Low Diastolic Blood Pressure is Associated with Angina in Patients with Chronic Coronary Artery Disease




APPEAR was an observational cohort study

*J Am Coll Cardiol. 2018 Sep 11; 72(11*

# Low Diastolic Blood Pressure is Associated with Angina in Patients with Chronic Coronary Artery Disease



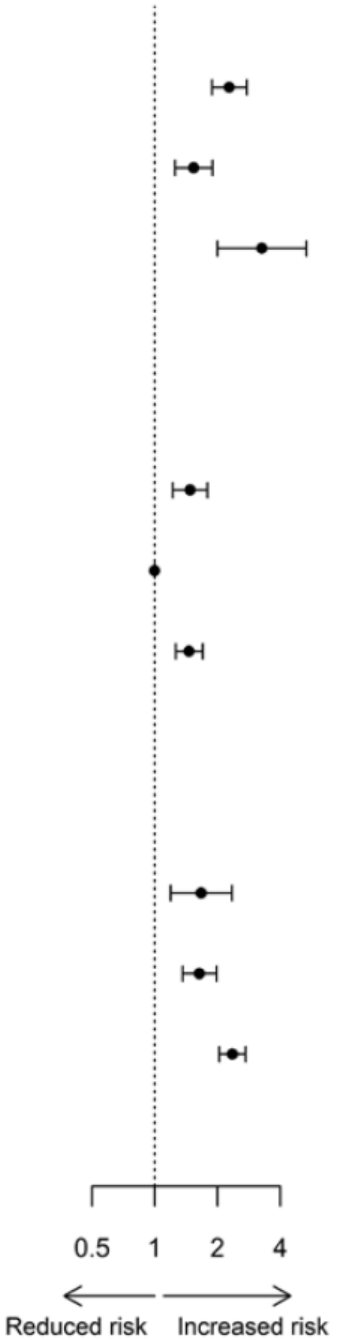

several potential limitations …
First and foremost, the cross-sectional design of our study means that we cannot establish the direction of causality in the association between low DBP and angina risk.
This is evident as patients who have more angina are treated more aggressively with beta-blockers and calcium channel blockers for their angina, which also lowers DBP. While we saw minimal attenuation in the association of DBP with angina after adjustment for these medications, we were unable to examine doses of medications or to monitor patients longitudinally to better understand this association. Future studies are needed to better disentangle this potential source of confounding.

APPEAR was an observational cohort study

*J Am Coll Cardiol. 2018 Sep 11; 72(11*

# Cardiovascular death or myocardial infarction and DBP subgroups cross-classified with SBP subgroups.

| | No.events / No. patients (%) | HR (95% CI); P Value |
|---|---|---|
| **SBP <120 mm Hg** | | |
| DBP <70 mm Hg | 152 / 1073 (14.2%) | 2.28 (1.88-2.76); p < 0.001 |
| DBP 70-79 mm Hg | 120 / 1465 (8.2%) | 1.54 (1.25-1.89); p < 0.001 |
| DBP ≥ 80 mm Hg | 17 / 149 (11.4%) | 3.27 (2.00-5.33); p < 0.001 |
| **SBP 120 - 139 mm Hg** | | |
| DBP <70 mm Hg | 152 / 1662 (9.1%) | 1.48 (1.22-1.79); p < 0.001 |
| DBP 70-79 mm Hg | 408 / 7785 (5.2%) | 1.00 (-) |
| DBP ≥ 80 mm Hg | 328 / 5106 (6.4%) | 1.46 (1.26-1.70); p < 0.001 |
| **SBP ≥ 140 mm Hg** | | |
| DBP <70 mm Hg | 38 / 309 (12.3%) | 1.67 (1.19-2.35); p = 0.0031 |
| DBP 70-79 mm Hg | 153 / 1589 (9.6%) | 1.64 (1.36-1.98); p < 0.001 |
| DBP ≥ 80 mm Hg | 377 / 3501 (10.8%) | 2.36 (2.04-2.72); p < 0.001 |




*CLARIFY registry*
*Hypertension. 2018*

## Novelty and Significance

### What Is New?

- In this large population of patients with coronary artery disease and treated hypertension, we show for the first time that the J-shaped relationship between diastolic blood pressure (BP) and cardiovascular events persists in patients with the lowest-risk pulse pressure.

### What Is Relevant?

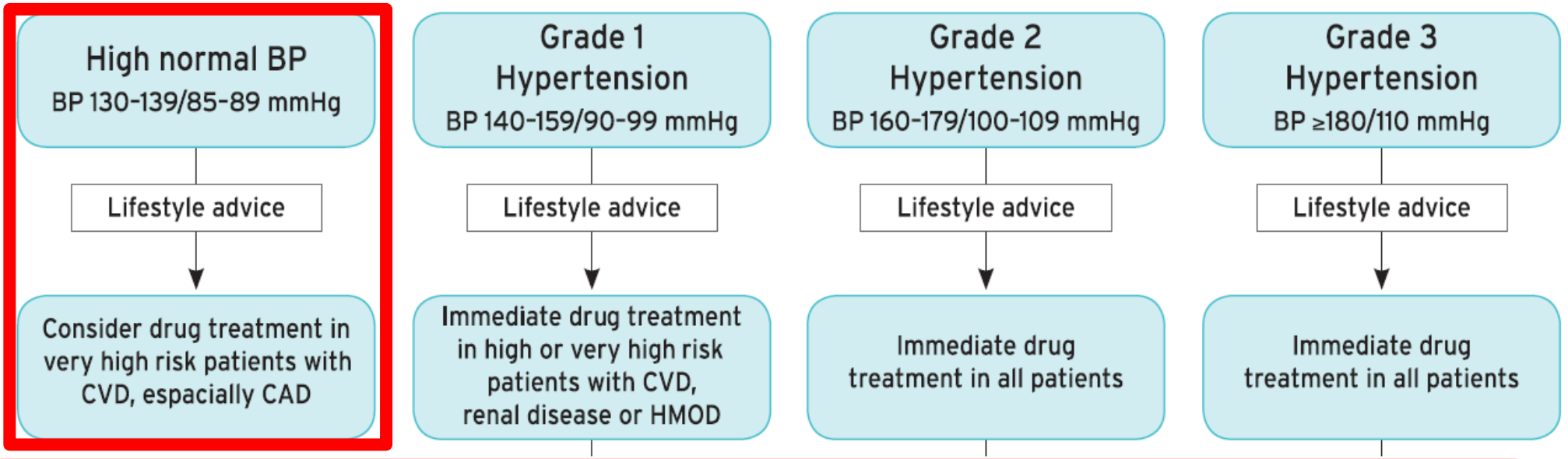
- The increased risk observed at low diastolic BP is not an epiphenomenon of increased pulse pressure.
- Although reverse causality cannot be ruled out by our observational study, the alternative hypothesis of a compromised myocardial perfusion associated with low diastolic BP seems to be a likely explanation for the J-curve of diastolic BP.

### Summary

In 22 672 hypertensive patients from the CLARIFY registry (Prospective Observational Longitudinal Registry of Patients With Stable Coronary Artery Disease), the J-shaped relationship between diastolic BP and the primary outcome (cardiovascular death or myocardial infarction) remained in patients within the lowest-risk pulse pressure range (45–65 mm Hg), with adjusted hazard ratios of 1.53, 1.00, and 1.54 in the <70, 70 to 79 (reference), and ≥80 mm Hg diastolic BP subgroups, respectively.

*CLARIFY registry*
*Hypertension. 2018*

# Initiation of blood pressure-lowering treatment (lifestyle changes and medication) at different initial office blood pressure levels




| | | |
|---|---|---|
| In patients with high–normal BP (130–139/85–89 mmHg):<br>• Lifestyle changes are recommended.[17,35] | I | A |
| • Drug treatment may be considered when their CV is very high due to established CVD, especially CAD.[217] | IIb | A |

*2018 ESC/ESH Guidelines*

**Table 19** Summary of office blood pressure thresholds for treatment

| Age group | Office SBP treatment threshold (mmHg) | | | | | Office DBP treatment threshold (mmHg) |
|---|---|---|---|---|---|---|
| | Hypertension | + Diabetes | + CKD | + CAD | + Stroke/TIA | |
| 18 - 65 years | ≥140 | ≥140 | ≥140 | ≥140[a] | ≥140[a] | ≥90 |
| 65 - 79 years | ≥140 | ≥140 | ≥140 | ≥140[a] | ≥140[a] | ≥90 |
| ≥80 years | ≥160 | ≥160 | ≥160 | ≥160 | ≥160 | ≥90 |
| **Office DBP treatment threshold (mmHg)** | ≥90 | ≥90 | ≥90 | ≥90 | ≥90 | |

BP = blood pressure; CAD = coronary artery disease; CKD = chronic kidney disease; DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

[a]Treatment may be considered in these very high-risk patients with high–normal SBP (i.e. SBP 130–140 mmHg).

*2018 ESC/ESH Guidelines*

**Table 23** Office blood pressure treatment target range

| Age group | Office SBP treatment target ranges (mmHg) | | | | | Office DBP treatment target range (mmHg) |
|---|---|---|---|---|---|---|
| | Hypertension | + Diabetes | + CKD | + CAD | + Stroke[a]/TIA | |
| 18 - 65 years | **Target to 130** *or lower if tolerated* Not <120 | **Target to 130** *or lower if tolerated* Not <120 | **Target to <140 to 130** *if tolerated* | **Target to 130** *or lower if tolerated* Not <120 | **Target to 130** *or lower if tolerated* Not <120 | 70–79 |
| 65 - 79 years[b] | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | 70–79 |
| ≥80 years[b] | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | **Target to 130-139** *if tolerated* | 70–79 |
| **Office DBP treatment target range (mmHg)** | 70–79 | 70–79 | 70–79 | 70–79 | 70–79 | |



CAD = coronary artery disease; CKD = chronic kidney disease (includes diabetic and non-diabetic CKD); DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

[a]Refers to patients with previous stroke and does not refer to blood pressure targets immediately after acute stroke.

[b]Treatment decisions and blood pressure targets may need to be modified in older patients who are frail and independent.

*2018 ESC/ESH Guidelines*

# Therapeutic strategies in hypertensive patients with CAD

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| In patients with CAD receiving BP-lowering drugs, it is recommended: | | |
| • To target SBP to ≤ 130 mmHg if tolerated, but not <120 mmHg.[2,496] | I | A |
| • In older patients (aged ≥65 years), to target to an SBP range of 130–140 mmHg.[2,496] | I | A |
| • To target DBP to <80 mmHg, but not <70 mmHg. | I | C |
| In hypertensive patients with a history of myocardial infarction, beta-blockers and RAS blockers are recommended as part of treatment.[503] | I | A |
| In patients with symptomatic angina, beta-blockers and/or CCBs are recommended.[503] | I | A |

*2018 ESC/ESH Guidelines*